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NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
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NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
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NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
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NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment

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L1    10122901 METHOD

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L2          150 L1 AND INHIBIT IGE

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L3            0 L2 AND "ANTI HUMAN CD23"

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L4            1 CHIMERIC HUMAN CD23

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L4   ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946  Document No.: PREV200200370946. Antibodies against the stalk
     region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis.
     Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew;
     Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia
     Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298
     USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239.
     http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of
     Professional Research Scientists on Experimental Biology New Orleans,
     Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB   The stalk region of human CD23 comprising a.a. 48-158 was expressed in E.
     coli and purified. In addition a chimeric human
     CD23 was prepared consisting of the extracellular region of CD23
     linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were
     produced in rabbits and shown to block binding of IgE to CD23 both on cell
     surfaces as well as the interaction of LZ-CD23 with IgE in an ELISA based
     assay. The antisera was also shown to inhibit IgE synthesis in an
     anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose
     dependent and essentially complete blockage of IgE production was seen at
     a relatively low dose of anti-stalk. FACS analysis using CD23+B
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lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

=> s l2 and CD23 antibody
L5 1 L2 AND CD23 ANTIBODY

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L6 2321935 ANTIBOD?

=> s l6 and CD23
L7 3178 L6 AND CD23

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L8 16 L7 AND HUMANIZED

=> s l8 and primate
L9 1 L8 AND PRIMATE

=> d l9 cbib abs

L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FceRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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L10 12 DUP REMOVE L9 (4 DUPLICATES REMOVED)

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L10 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2002:221424 Document No. 136:244644 Combination therapy for treatment of autoimmune diseases using B cell depleting immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 86 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,

NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010919. PRIORITY: US 2000-PV257147 20001220.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L10 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2002036168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M., M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized** monoclonal Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L10 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L10 ANSWER 4 OF 12 MEDLINE DUPLICATE 1

2001262398 Document Number: 21203341. PubMed ID: 11307028.
Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. [Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl] . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcepsilonRI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized** anti-IgE mAb Hu-901 can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "**humanized**" monoclonal **antibodies** and sol. receptors, receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L11 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:361519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Lebeer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2001028579 A1 20010426, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ,

EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (IgE Fc receptor type I and **CD23**, expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized** anti-**CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, **humanized** IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.95 × 10⁶ M⁻¹ s⁻¹ and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:614934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko

(Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FceRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L10 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L10 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b CD18 and CD11c CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of

monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L10 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredscho, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940118.
AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s monkey anti human CD23
L11 0 MONKEY ANTI HUMAN CD23

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FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON 05 JUL 2002
L1 10122901 S METHOD
L2 150 S L1 AND INHIBIT IGE
L3 0 S L2 AND "ANTI HUMAN CD23"
L4 1 S CHIMERIC HUMAN CD23
L5 0 S L2 AND CD23 ANTIBODY
L6 2321935 S ANTIBOD?
L7 3178 S L6 AND CD23
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L11 0 S MONKEY ANTI HUMAN CD23

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L13 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
2001150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-**CD23** monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao W; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000 Feb 22 2 131-41. Journal code: 7904795. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
AB **CD23**, the low affinity receptor for IgE FcvarepsilonRII , is

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     involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal
     antibodies to human CD23 were generated from cynomolgus
     macaques immunized with purified soluble CD23 (sCD23). Four of
     the five primate antibodies blocked the binding of IgE complexes
     to CD23 positive cells and also inhibited the production of IgE
     in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC).
     The variable domains of several primate antibodies were utilized
     to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal
     antibodies. PRIMATIZED((R)) p5E8G1, containing human
     gamma 1 constant region, inhibited
     IgE production in vitro as efficiently as the parent primate
     antibody, but the human gamma 4 constant version, PRIMATIZED((R))
     p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did
     not inhibit IgE production but did interfere with IgE inhibition by the
     intact anti-CD23 antibody in a dose dependent fashion.
     The murine monoclonal antibody MHM6 recognizes human
     CD23 at a different epitope than primate antibody 5E8,
     and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of
     p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These
     data imply that the mechanism by which anti-CD23
     antibodies inhibit IgE production requires cross-linking of
     CD23 to an IgG receptor. These data also imply that neither
     bivalent cross-linking of CD23 alone or inhibition of
     CD23 binding to its natural ligands is sufficient to inhibit IgE
     production.


=> s primatized CD23
L14          0 PRIMATIZED CD23

=> d his

     (FILE 'HOME' ENTERED AT 13:19:26 ON 05 JUL 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON
     05 JUL 2002
L1     10122901 S METHOD
L2          150 S L1 AND INHIBIT IGE
L3            0 S L2 AND "ANTI HUMAN CD23"
L4            1 S CHIMERIC HUMAN CD23
L5            0 S L2 AND CD23 ANTIBODY
L6      2321935 S ANTIBOD?
L7         3178 S L6 AND CD23
L8           16 S L7 AND HUMANIZED
L9            1 S L8 AND PRIMATE
L10          12 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L11           0 S MONKEY ANTI HUMAN CD23
L12           5 S L7 AND HUMAN GAMMA 1 CONSTANT REGION
L13           1 DUP REMOVE L12 (4 DUPLICATES REMOVED)
L14           0 S PRIMATIZED CD23

=> s 17 and human IgG1 Fc
L15           3 L7 AND HUMAN IGG1 FC

=> dup remove 115
PROCESSING COMPLETED FOR L15
L16           1 DUP REMOVE L15 (2 DUPLICATES REMOVED)

=> d 116 cbib abs

L16  ANSWER 1 OF 1     MEDLINE                               DUPLICATE 1
92325512  Document Number: 92325512.     PubMed ID: 1379[illegible]75.   Soluble forms of
     CD40 inhibit biologic responses of human B cells. Fanslow W C; Anderson D
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M; Grabstein K H; Clark E A; Cosman D; Armitage R J. Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101. : JOURNAL OF IMMUNOLOGY, 1992 Jul 15, 149 (2) 655-60. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 28-kDa molecule and a 57-kDa Fc fusion protein containing the **human IgG1 Fc** region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb G28-5. Similarly, G28-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

=> s l7 and humanized
L17 16 L7 AND HUMANIZED

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 12 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d l18 1-12 cbib abs

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002236168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M., M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 45-49 2002.
Refs: 25.
ISSN: 1335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized** monoclonal

Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L18 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
20001262398 Document Number: 21203341. PubMed ID: 11307028.
Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcepsilonRI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized** anti-IgE mAb Hu-901 can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data

clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.
Copyright 2001 S. Karger AG, Basel

L18 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.
AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with **"humanized"** monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L18 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.
AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (IgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-21) anti-IgE **antibody** and fragments as allergy inhibitors.

L18 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG,

CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-29624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized** anti-**CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L18 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, **humanized** IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE FceRII/**CD23**, and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L18 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:391154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE,

KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS

1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredscho, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940118.

AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s anti human CD23
L19 9 ANTI HUMAN CD23

=> dup remove l19

PROCESSING COMPLETED FOR L19
L20 5 DUP REMOVE L19 (3 DUPLICATES REMOVED)

=> d l20 1-5 cbib abs

L20 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 **anti-human CD23** monoclonal antibodies. Reff, Mitchell E. [1]; Kloetzer, William S.; Nakamura, Takehiko. [1] San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011139 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB **Anti-human CD23** monoclonal antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced IgE production by B-cells significantly greater than antibodies containing other constant domains.

L20 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. Reff, Mitchell R.; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and **Anti-human CD23** antibody and immunoadhesin in Desmond marked CHO cells was achieved.

L20 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
1999:674934 Document No. 131:315723 Gamma-1 and gamma-3 **anti-human CD23** monoclonal antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO

9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English. CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal antibodies which specifically bind human CD23, the low affinity receptor for IgE (FceRII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L20 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of IgE production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect Immunofluorescence of monoclonal antibodies, for IgE, IL-4 with ELISA, for IL-2 with F12-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with **anti human CD23** McAb. The mechanism of T cells and cytokines in the regulation of IgE production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of IgE, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant IgE difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of IgE antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L20 ANSWER 5 OF 5 MEDLINE DUPLICATE 1

91010830 Document Number: 91010830. PubMed ID: 1698879. A bioassay for the measurement of human interleukin-4. Siegel J P; Mostowski H S. (Division of Cytokine Biology, Center for Biologics Evaluation and Research, FDA, Bethesda, MD.) JOURNAL OF IMMUNOLOGICAL METHODS, 1990 Sep 14, 132 (2) 287-95. Journal code: 1305441. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB We have developed a bioassay for human IL-4 based upon its ability to upregulate CD23 (low affinity IgE receptor) expression. Ramos, a B lymphocyte line derived from a Burkitt lymphoma, was repetitively subcloned yielding a clone, Ramos.G6.C10, which is several fold more sensitive to this effect of IL-4. In microtiter plates cells were cultured for 48 h in the presence of dilutions of recombinant human IL-4 or samples, and then stained with murine **anti-human CD23** and goat anti-mouse IgG-FITC. IL-4 induced an eight-fold increase (8) channel shift) in fluorescence intensity as measured by flow cytometry. Significant effects were observed at an IL-4 concentration of 5[illegible] pg/ml and increased with concentrations up to [illegible] pg/ml. Inter- and intra-assay coefficients of variation were [illegible] and [illegible] respectively. The

bioassay showed good specificity for IL-4; however, tumor necrosis factors alpha and beta, at optimal concentrations, gave readings barely at the threshold of detection.

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L21       1255 (REMPEL F?/AU OR BROOKS K?/AU)

=> s l21 and anti CD23
L22          0 L21 AND ANTI CD23

=> s l21 and antibody
L23         83 L21 AND ANTIBODY

=> s l23 and CD23
L24          0 L23 AND CD23

=> s l23 and IgE
L25          1 L23 AND IGE

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L25  ANSWER 1 OF 1     MEDLINE
95048595  Document Number: 95048595.    PubMed ID: 7525472.   B-1 cells in
     systemic autoimmune responses: IgM+, Fc epsilon Rdull B cells are lost
     during chronic graft-versus-host disease but not in murine AIDS or
     collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M;
     Brooks K H. (Department of Microbiology, Michigan State
     University, East Lansing 48824. ) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug)
     23 (4-5) 293-311.  Journal code: 8504629. ISSN: 0882-0139. Pub. country:
     United States. Language: English.
AB   The potential role of B-1 cells (i.e. the CD5+ B cell and "sister" B cell
     subsets) in autoimmunity is controversial. CD5+ B cells have been shown to
     secrete antibodies of similar specificity as those found in many
     systemic autoimmune diseases; in addition, increases in CD5+ B cell
     frequency have been reported in patients suffering from rheumatoid
     arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent
     diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are
     due to expansion of B-1 lineage cells in the human or due to
     activation-induced expression of CD5 by conventional B cells is unclear.
     In the present study, we used three murine models of systemic
     autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic
     graft-versus-host disease (cGvHD), and collagen-induced arthritis (CIA) to
     determine whether increases in B-1 cell frequency are universally seen in
     models of autoimmunity which are mechanistically distinct. In contrast to
     the aforementioned human systemic autoimmune diseases which exhibit an
     increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined
     in all three murine models of systemic autoimmune disease. Even though
     there was a decrease in the frequency of CD5+ B cells there was no change
     in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B
     cell frequency was due to increases in either T cells, conventional Fc
     epsilon R+ B cells, or both. The only actual decline in a B cell subset
     was the loss of IgM+, Fc epsilon Rdull cells in both the spleen and
     peritoneal cavity of mice undergoing a chronic graft-versus-host reaction.
     Therefore, our data suggests that expansion of the B-1 subset does not
     occur as a general feature of murine systemic autoimmune disease. These
     observations, consistent with previous studies of Ig gene usage in
     autoreactive antibodies, support the view that expansion and
     differentiation of the CD5+ B cell subset is not a central event leading
     to autoantibody production.

=> dup remove l23
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PROCESSING COMPLETED FOR L23
L26 37 DUP REMOVE L23 (46 DUPLICATES REMOVED)

=> d l26 1-37 cbib abs

L26 ANSWER 1 OF 37 MEDLINE DUPLICATE 1
2002200719 Document Number: 21904109. PubMed ID: 11906504. Increased expression of the neuronal glutamate transporter (EAAT3/EAAC1) in hippocampal and neocortical epilepsy. Crino Peter B; Jin Hong; Shumate Melissa D; Robinson Michael B; Coulter Douglas A; **Brooks-Kayal Amy R.** (PENN Epilepsy Center, Department of Neurology, University of Pennsylvania, Philadelphia, Pennsylvania, USA.) EPILEPSIA, (2002 Mar) 43 (3) 211-8. Journal code: 2983306R. ISSN: 0013-9580. Pub. country: United States. Language: English.

AB PURPOSE: To define the changes in gene and protein expression of the neuronal glutamate transporter (EAAT3/EAAC1) in a rat model of temporal lobe epilepsy as well as in human hippocampal and neocortical epilepsy. METHODS: The expression of EAAT3/EAAC1 mRNA was measured by reverse Northern blotting in single dissociated hippocampal dentate granule cells from rats with pilocarpine-induced temporal lobe epilepsy (TLE) and age-matched controls, in dentate granule cells from hippocampal surgical specimens from patients with TLE, and in dysplastic neurons microdissected from human focal cortical dysplasia specimens. Immunolabeling of rat and human hippocampi and cortical dysplasia tissue with EAAT3/EAAC1 **antibodies** served to corroborate the mRNA expression analysis. RESULTS: The expression of EAAT3/EAAC1 mRNA was increased by nearly threefold in dentate granule cells from rats with spontaneous seizures compared with dentate granule cells from control rats. EAAT3/EAAC1 mRNA levels also were high in human dentate granule cells from patients with TLE and were significantly elevated in dysplastic neurons in cortical dysplasia compared with non-dysplastic neurons from postmortem control tissue. No difference in expression of another glutamate transporter, EAAT2/GLT-1, was observed. Immunolabeling demonstrated that EAAT3/EAAC1 protein expression was enhanced in dentate granule cells from both rats and humans with TLE as well as in dysplastic neurons from human cortical dysplasia tissue. CONCLUSIONS: Elevations of EAAT3/EAAC1 mRNA and protein levels are present in neurons from hippocampus and neocortex in both rats and humans with epilepsy. Upregulation of EAAT3/EAAC1 in hippocampal and neocortical epilepsy may be an important modulator of extracellular glutamate concentrations and may occur as a response to recurrent seizures in these cell types.

L26 ANSWER 2 OF 37 MEDLINE DUPLICATE 2
20011183114 Document Number: 21128425. PubMed ID: 11233905. Improved flow cytometric detection of HLA alloantibodies using pronase: potential implications in renal transplantation. Vaidya S; Cooper T Y; Avandsalehi J; Barnes T; **Brooks K;** Hymel P; Noor M; Sellers R; Thomas A; Stewart D; Dailer J; Fish J C; Gugliuzza K K; Bray R A. (Department of Pathology, University of Texas Medical Branch, Galveston 77555-0178, USA.) TRANSPLANTATION, (2001 Feb 15) 71 (3) 422-9. Journal code: 0132144. ISSN: 0041-1337. Pub. country: United States. Language: English.

AB BACKGROUND: Flow cytomeric crossmatch (FCXM) has grown in popularity and has become the "standard of practice" in many programs. Although FCXM is the most sensitive method for detecting alloantibody, the B cell FCXM has been problematic. Difficulties with the B cell FCXMs have been centered around high nonspecific fluorescence background owing to Fc-receptors present on the B cells and autoantibodies. To improve the specificity and sensitivity of the B cell FCXM, we utilized the proteolytic enzyme pronase to remove Fc receptors from lymphocytes before their use in FCXM. METHODS: Lymphocytes isolated from peripheral blood, spleen, or lymph nodes were treated with pronase and then used in a three-color FCXM. A total of 167 T- and B cell FCXMs using pronase-treated and untreated cells were performed. Testing used serial dilutions of HLA allosera (22 class I and 6

class II), with the titer of each **antibody** at one dilution past the titer at which the complement-mediated cytotoxicity anti-human globulin crossmatch became negative. RESULTS: After pronase treatment, the actual channel values of the negative control in both T cell and B cell FCXMs declined from 78+/-10 to 57+/-4 (P<0.05) and 107+/-11 to 49+/-3 (P<0.00001), respectively. Pronase treatment resulted in improved sensitivity of the T and B cell FCXM in detecting class I **antibody** by 20% and 80%, respectively. In no instance was a false-positive reaction observed. In this study, pronase treatment improved the specificity of B cell FCXM for detecting class II **antibodies** from 75% to 100% (P=0.03). In no instance was a false-negative reaction recorded. Lastly, on the basis of these observations we re-evaluated three primary transplant recipients who lost their allografts because of accelerated rejection. One of the patients was transplanted across negative T and B cell FCXM, whereas the other two patients were transplanted across a positive T cell, but negative B cell, FCXM. After pronase treatment, T and B cell FCXMs of each patient became strongly positive, and donor-specific anti-HLA class I **antibody** was identi. fied in each case. CONCLUSION: Utilization of pronase-treated lymphocytes improves both the sensitivity and specificity of the FCXM.

L26 ANSWER 3 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:495043 Document No.: PREV200000495164. Influenza vaccine may induce auto-reactive IgG **antibodies** detectable in flow cytometry crossmatches. Cooper, T. Y. (1); Avandsalehi, J. (1); Hymel, P. (1); Barnes, T. (1); Thomas, A. (1); Sellers, R. (1); **Brooks, K. (1)**; Noor, M. (1); Qiu, S. M. (1); Gugliuzza, K. (1); Daller, J. (1); Vaidya, S. (1). (1) Departments of Pathology and Surgery, University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (2000) Vol. 61, No. Supplement 2, pp. S80. print. Meeting Info.: 26th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Lake Buena Vista, Florida, USA October 10-14, 2000 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English. Summary Language: English.

L26 ANSWER 4 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:472830 Document No.: PREV199900472830. High background fluorescence may contribute to false negative B lymphocyte flow cytometry crossmatches. Cooper, T. (1); Hymel, P. (1); Thomas, A. (1); **Brooks, K. (1)**; Avandsalehi, J. (1); Stewart, D.; Bray, R.; Vaidya, S. (1). (1) Department of Pathology, The University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (1999) Vol. 60, No. SUPPL. 2, pp. S140. Meeting Info.: 25th Annual Meeting of the American Society for Histocompatibility and Immunogenetics New Orleans, Louisiana, USA October 20-24, 1999 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 5 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:483339 The Genuine Article (R) Number: ZU842. Modulation of IL-1 beta, IL-6 and TNF-alpha secretion and mRNA expression by the trichothecene vomitoxin in the RAW 264.7 murine macrophage cell line. Wong S S; Zhou H R; MarinMartinez M L; **Brooks K**; Pestka J J (Reprint). MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT BLDG, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL CTR FOOD SAFETY & TOXICOL, E LANSING, MI 48824. FOOD AND CHEMICAL TOXICOLOGY MAY 1998 Vol. 36, No. 5, pp. 419-429. Publisher: PERGAMON-ELSEVIER SCIENCE LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0278-6915. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND TALL FORMATS
AB Oral exposure of mice to vomitoxin (VT) has been previously shown to

enhance gene expression of several cytokines associated with macrophage activation. Here, the effects of exposure to VT in vitro on cytokine secretion and mRNA expression were determined in the murine macrophage cell line RAW 264.7. Enzyme-linked immunosorbent assay (ELISA) of supernatants revealed that significant increases in secreted tumour necrosis factor alpha (TNF-alpha) were observed 2 days after exposure to VT at. 100 ng/ml and 250 ng/ml, both with and without lipopolysaccharide (LPS) activation. While VT did not affect IL-6 secretion in the absence of LPS, significantly increased IL-6 production was observed in culture supernatants after 1, 2 and 5 days of exposure to VT at 250 ng/ml in the presence of LPS. Soluble IL-1 beta was not detected in control or VT-treated cell cultures with or without LPS activation. Immunochemical staining of intracellular cytokines in conjunction with flow cytometric analysis was used to detect the effects of VT on the percentage of positive cells and output per cell. The percentage of cells that produced intracellular TNF-alpha were significantly increased at 100 and 250 ng/ml VT with and without LPS whereas increased IL-6 output per cell was observed at 100 and 250 ng/mI VT with LPS. To assess the effects of VT on cytokine mRNA expression, RAW 264.7 cells were analysed semi-quantitatively using reverse transcription-polymerase chain reaction(RT-PCR) in conjunction with Southern hybridization analysis. Elevated TNF-alpha mRNA was observed at 100 and 250 ng VT/ml at 6 and 24 hr in the absence of LPS. With the addition of LPS, superinduction of TNF-alpha was not observed in the presence of VT. Increased IL-1 beta and IL-6 mRNAs were observed at 100 and 250 ng VT/ml at 24 hr in the presence of LPS. These results demonstrated that VT could superinduce both cytokine secretion and mRNA levels in macrophage cultures.

L26 ANSWER 6 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:182785 The Genuine Article (R) Number: YZ186. Role of macrophages in elevated IgA and IL-6 production by Peyer's patch cultures following acute oral vomitoxin exposure. Yan D (Reprint); Zhou H R; **Brooks K H;** Pestka J J. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL FOOD SAFETY & TOXICOL, E LANSING, MI 48824. TOXICOLOGY AND APPLIED PHARMACOLOGY (FEB 1998) Vol. 148, No. 2, pp. 261-273. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS. 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0041-008X. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Oral vomitoxin (VT) exposure in mice results in elevated cytokine gene expression, increased production of IgA, and IgA nephropathy, To determine the potential role of macrophages (M phi) in these effects, an ex vivo model was devised whereby Peyer's patch (PP) and spleen cells were prepared from mice 2 h after oral exposure to 0 or 25 mg/kg body wt VT, cultured, and then evaluated for IgA and cytokine IL-6 production, Both PP and, to a lesser extent, spleen cells from treatment mice produced more IgA over a 7-day period than did corresponding control cells when cultured without a costimulus or in the presence of either phorbol myristate acetate plus ionomycin (PMA + ION) or lipopolysaccharide (LPS); IgA elevation was most marked in LPS-treated cultures. The VT effect was completely ablated in PP cultures that were depleted of M phi but not in M phi-depleted spleen cultures, VT exposure similarly increased production of IL-6, an important helper factor for IgA secretion, in LPS-stimulated PP and spleen cell cultures, IL-6 production was also ablated by M phi depletion, A potential costimulatory role for M phi was further suggested because both IgA and IL-6 production increased when M phi-depleted PP cells from VT-treated animals were cocultured with peritoneal M phi from VT-treated animals, Similar effects were observed when an analogous ex vivo approach was used with purified PP B cells and peritoneal M phi. PP B cells from control animals also secreted elevated levels of IgA when

cocultured with splenic CD4(+) cells from VT-treated animals, thus confirming previous studies showing that T cell help also contributes to increased IgA production. Potential roles for soluble mediators and cell contact in this process were suggested when IgA production was measured in cultures of PP cells separated from VT-treated M phi by a semipermeable membrane. Taken together, these and previous results suggest that M phi may play a key mechanistic role in elevated IgA production and IgA nephropathy in VT-exposed mice. (C) 1998 Academic Press.

L26 ANSWER 7 OF 37 MEDLINE DUPLICATE 3
1998432619 Document Number: 98432619. PubMed ID: 9761452. The glutamate transporter, GLT-1, is expressed in cultured hippocampal neurons. **Brooks-Kayal A R**; Munir M; Jin H; Robinson M B. (Department of Neurology, Children's Hospital of Philadelphia, Children's Seashore House, University of Pennsylvania, 19104, USA.. kayal@email.chop.edu) . NEUROCHEMISTRY INTERNATIONAL, (1998 Aug) 33 (2) 95-100. Journal code: 8006959. ISSN: 0197-0186. Pub. country: ENGLAND: United Kingdom. Language: English.

AB There are multiple subtypes of Na+-dependent glutamate transporters. Several studies suggest that EAAC1 and EAAT4 are expressed in neurons, while GLT-1 and GLAST expression is thought to be restricted to glia. In the present study, expression of GLT-1 and EAAC1 was examined in cultured rat hippocampal neurons using single cell mRNA amplification and immunocytochemistry with subtype specific **antibodies**. GLT-1 and EAAC1 mRNAs were observed in all neurons examined. Neuronal phenotype was confirmed in these cells by expression of neurofilament (NF-L) mRNA and absence of glial fibrillary acidic protein (GFAP) mRNA. EAAC1 immunoreactivity was observed in essentially all cells which expressed neuron specific enolase (NSE) and GLT-1 immunoreactivity was detected in the majority (approximately 90%) of NSE-positive cells. Consistent with the glial expression of GLT-1, GLT-1 immunoreactivity was also observed in NSE-negative cells. These studies provide evidence that GLT-1 expression is not intrinsically restricted to glial cells, but can occur in neurons under certain circumstances.

L26 ANSWER 8 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:470990 Document No.: PREV199800470990. Impact of positive flow crossmatches on primary renal transplants. Cooper, Todd; Vaidya, Smita; Asfour, M. Ayman; Avandsalehi, Jeanne; Barnes, Titus; **Brooks, Karl** ; Lopez, Sheila; Partlow, David; Sellers, Racheal; Thomas, Alice. Univ. Tex. Med. Branch, Galveston, TX USA. Human Immunology, (1998) Vol. 59, No. SUPPL. 1, pp. 7. Meeting Info.: 24th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Vancouver, British Columbia, Canada October 10-15, 1998 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 9 OF 37 MEDLINE DUPLICATE 4
97418734 Document Number: 97418734. PubMed ID: 9274810. Potential role for IL-5 and IL-6 in enhanced IgA secretion by Peyer's patch cells isolated from mice acutely exposed to vomitoxin. Yan D; Zhou H R; **Brooks K H**; Pestka J J. (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824, USA. TOXICOLOGY, (1997 Sep 26) 122 (1-2) 145-59. Journal code: 0361055. ISSN: 0300-483X. Pub. country: Ireland. Language: English.

AB Dietary exposure to vomitoxin (VT) results in hyperelevated serum IgA and IgA nephropathy in mice. To assess the possible role of cytokines in this IgA dysregulation, the effects of a single oral exposure in B6C3F1 male mice to 1, 5 or 25 mg/kg BW VT on production of IgA and cytokines in Peyer's patch (PP) and spleen cell cultures were evaluated. IgA levels were increased significantly in PP cell cultures prepared from mice at 2 or 24 h after oral exposure to VT and subsequently stimulated with phorbol myristate acetate (PMA) and ionomycin (ION) or with lipopolysaccharide (LPS). Significant effects on IgA production were not observed in spleen

cell cultures. Since cytokines such as IL-2, IL-4, IL-5 and IL-6 have been shown to promote IgA production, the effect of the same VT exposure regimen on secretion of these mediators was determined in PP and spleen cultures. Supernatant IL-2 and IL-4 levels were unaffected by the prior treatment of animals with VT. In contrast, IL-5 levels were increased significantly in 7-day PP cell cultures obtained 2 h after VT exposure both with and without PMA + ION exposure but not in other cultures. IL-6 levels were increased significantly in LPS-treated cultures prepared from PP at 2 and 24 h following exposure to VT. IL-6 levels were also elevated significantly in both PMA + ION or LPS treated cultures from spleen isolated at 2 h but not 24 h post VT exposure. To determine whether IL-5 or IL-6 play a role in IgA hyperelevation in vitro, PP and spleen cells from mice obtained 2 h after exposure to 25 mg/kg VT were cultured in the presence of neutralizing cytokine **antibodies** (Abs) and IgA production was monitored. Consistent with IL-5's previously documented role in IgA production, anti-IL-5 decreased IgA levels to background in cultures of both control and VT-exposed PP or spleen cells in the presence of either PMA + ION or LPS. Similar results were seen with addition of anti-IL-6. IgA levels were decreased to a lesser extent in PP cells cultured with LPS and in spleen cells cultured with PMA + ION from VT-exposed mice to which anti-IL-2 Ab was added. Thus, the potential for enhanced IgA production exists in lymphocytes as early as 2 h and as late as 24 h after a single oral exposure to VT and this may be related to the increased capacity to secrete helper cytokines of T cell and macrophage origin. Taken together, the results suggest that the superinduction of cytokine expression may, in part, be responsible for upregulation of IgA secretion in mice exposed orally to VT.

L26 ANSWER 10 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:62941 Document No.: PREV199800062941. Acute rejection of a living related kidney associated with positive T-cell flow cytometry crossmatch. Cooper, T. Y.; Sellers, R. B.; Asfour, M. A.; Lopez, S. B.; Moller-Nichols, M.; Barnes, T. H.; **Brooks, K.**; Partlow, D.; Avandsalehi, J.; Thomas, A.; Vaidya, S.. Dep. Pathol., Univ. Texas Med. Branch, Galveston, TX USA. Human Immunology, (1997) Vol. 55, No. SUPPL. 1, pp. 75. Meeting Info.: 23rd Annual Meeting of the American Society for Histocompatibility and Immunogenetics Atlanta, Georgia, USA October 14-19, 1997 The American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 11 OF 37 MEDLINE DUPLICATE 5
96022850 Document Number: 96022850. PubMed ID: 7549055. Clinical importance of pre-morteum blood lymphocytes in cadaver donor tissue typing. Vaidya S; Orchard P; Schroeder N; Haneke R; **Brooks K;** Thomas A; Corba A; Asfour A; Fish J C. (Department of Pathology, University of Texas Medical Branch, Galveston 77555-0546, U.S.A.) CLINICAL TRANSPLANTATION, (1995 Jun) 9 (3 Pt 1) 165-70. Journal code: 8710240. ISSN: 0902-0063. Pub. country: Denmark. Language: English.
AB We have refined our immunomagnetic bead (IM bead) procedures to isolate pure and viable lymphocyte subpopulation from pre-morteum (PM) blood for cadaver donor HLA typing, preliminary and final crossmatches (XMs). The results of 1220 XMs were compared using T/B lymphocytes isolated either from PM blood or spleen/lymphnode (SPLN) tissue. IM bead technique was used to isolate T/B cells from PM blood and nylon wool column (NWC) technique was used to isolate T/B cells from SPLN. When we compared the outcome of 84 T-cell crossmatches using T cells from PM blood or SPLN of 5 separate cadaver donors, NWC TXMs tended to be more falsenegative for high PRA (> 10%, total 511 XMs) as well as low PRA (< 10%, total 311 XMs) did not reach statistical significance. In contrast, NW BXM (42%) B XM were found to be far more false negative than IM bead BXM regardless of the PRA of the patients. In order to ensure that NWC BXMs were indeed false negative, 23 sera with known anti-DP **antibodies** were BXMed where antigen-specific B cells were isolated by both the techniques. Our

results showed that IM bead BXM identified the DR specificities greater than 90% of the time, the titers of ab specificities were stronger (1:8). In comparison, NWB cell XMs were weak titers 1:2), and the false negative rate for some ab was as high as 73%. Using IM bead and NWC techniques we compared our turnaround time (TAT) for cadaver donor typing, preliminary and final XMs.(ABSTRACT TRUNCATED AT 250 WORDS)

L26 ANSWER 12 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
94251909 EMBASE Document No.: 1994251909. In vitro effects of vomitoxin deoxynivalenol on T-cell interleukin production and IgA secretion.
Warner R.L.; **Brooks K.**; Pestka J.J.. Dept. of Food Sci./Human Nutrition, 234 G.M. Trout Bldg., Michigan State University,East Lansing, MI 48824-1224, United States. Food and Chemical Toxicology 32/7 (617-625) 1994.
ISSN: 0278-6915. CODEN: FCTOD7. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The exposure of lymphocyte cultures to vomitoxin was used to determine possible mechanism by which this naturally occurring toxin induces serum immunoglobulin A (IgA) elevation and IgA nephropathy in the mouse. Vomitoxin exposure within the range of 10 to 1000 ng/ml inhibited DNA synthesis, protein synthesis as well as IgA, IgG and IgM production in lymphocyte cultures prepared from the Peyer's patch (PP) and spleen. When purified B cells were cultured in the presence of vomitoxin, inhibition of IgA, IgG and IgM production was similarly observed. However, on 24-hr pulsed co-exposure to vomitoxin and the mitogen concanavalin A (ConA), CD4+/CD8+ cells were capable of inducing a three- to five-fold increase in production of IgA, but not IgG and IgM by cocultured B cells when compared with B cells cocultured with control T cells exposed to the mitogen only. When pulsed for 48 hr with ConA and toxin, CD4+ cells were similarly capable of causing a significant increase in IgA production by B cells. 48-hr pulsed exposure of CD4+ cells to ConA and vomitoxin resulted in significantly increased production of the T helper cytokines IL-4, IL-5 and IL-6 after 5 additional days of culture, compared with ConA-stimulated CD4+ cells alone. These results suggest that vomitoxin was capable of enhancing CD4+-mediated help for IgA production by B cells and that this could possibly be mediated by way of increased cytokine production.

L26 ANSWER 13 OF 37 MEDLINE DUPLICATE 7
94266212 Document Number: 94266212. PubMed ID: 8206429. Polyspecific and autoreactive IgA secreted by hybridomas derived from Peyer's patches of vomitoxin-fed mice: characterization and possible pathogenic role in IgA nephropathy. Rasooly L; Abouzied M M; **Brooks K H**; Pestka J J. (Department of Microbiology and Public Health, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1994 Apr) 32 (4) 337-48. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A total of 122 immunoglobulin (Ig) A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant **antibodies** were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenol that were representative of self and non-self antigens, approximately 95% of the monoclonal IgAs bound to at least one of the panel antigens and 80% bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition

in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 14 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
94:364738 The Genuine Article (R) Number: NQ428. POLYSPECIFIC AND AUTOREACTIVE IGA SECRETED BY HYBRIDOMAS DERIVED FROM PEYERS-PATCHES OF VOMITOXIN-FED MICE - CHARACTERIZATION AND POSSIBLE PATHOGENIC ROLE IN IGA NEPHROPATHY. RASOOLY L; ABOUZIED M M; **BROOKS K H**; PESTKA J J (Reprint). MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT BLDG, E LANSING, MI, 48824 (Reprint); MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI, 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL & PUBL HLTH, E LANSING, MI, 48824. FOOD AND CHEMICAL TOXICOLOGY (APR 1994) Vol. 32, No. 4, pp. 337. ISSN: 0278-6915. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant **antibodies** were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenol that were representative of self and non-self antigens, approximately 95% of the monoclonal IgAs bound to at least one of the panel antigens and 80% bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 15 OF 37 MEDLINE DUPLICATE 8
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in systemic autoimmune responses: IgM+, Fc epsilon Rdull B cells are lost during chronic graft-versus-host disease but not in murine AIDS or collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M; **Brooks K H**. (Department of Microbiology, Michigan State University, East Lansing 48824.) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug) 23 (4-5) 293-311. Journal code: 8804629. ISSN: 0882-0139. Pub. country: United States. Language: English.
AB The potential role of B-1 cells (i.e. the CD5+ B cell and "sister" B cell subsets) in autoimmunity is controversial. CD5+ B cells have been shown to secrete **antibodies** of similar specificity as those found in many systemic autoimmune diseases; in addition, increases in CD5+ B cell frequency have been reported in patients suffering from rheumatoid arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are due to expansion of B-1 lineage cells in the human or due to activation-induced expression of CD5 by conventional B cells is unclear. In the present study, we used three murine models of systemic autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic graft-versus-host disease (cGvHD), and collagen-induced arthritis (CIA) to determine whether increases in B-1 cell frequency are universally seen in models of autoimmunity which are mechanistically distinct. In contrast to the aforementioned human systemic autoimmune diseases which exhibit an

increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5+ B cells there was no change in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B cell frequency was due to increases in either T cells, conventional Fc epsilon R+ B cells, or both. The only actual decline in a B cell subset was the loss of IgM+, Fc epsilon Rdull cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5+ B cell subset is not a central event leading to autoantibody production.

L26 ANSWER 16 OF 37 MEDLINE DUPLICATE 9
94045239 Document Number: 94045239. PubMed ID: 8228625. Cytotoxic cell proteinase gene expression and cytolytic activity by anti-CD3-activated cytotoxic T lymphocytes is sensitive to cyclosporin A but is not dependent on interleukin-2 synthesis. Kaiser M; **Brooks-Kaiser J**; Fitzpatrick L; Bleackley R C; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Nov) 54 (5) 458-64. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.
AB We have examined the role of interleukin (IL) 2 in the expression of cytotoxic cell proteinases (CCP) 1 and 2, as well as in the induction of major histocompatibility complex (MHC)-unrestricted cytotoxic activity in murine T cell cultures following stimulation with anti-CD3 monoclonal **antibody**. A dramatic reduction in CCP-1 and CCP-2 gene expression and near absence of cytolytic activity was shown to occur in these cultures when the expression of IL-2 was inhibited by 10(-6) M cyclosporin A (CsA). The inhibitory effect of CsA could not be eliminated by the addition to culture of recombinant IL-2 at concentrations typically present in anti-CD3-stimulated T cell culture supernatants. Furthermore, when endogenous IL-2 (45-60 U/ml) present in anti-CD3-stimulated T cell cultures was neutralized with anti-mouse IL-2 **antibody** there was no effect on CCP-1 and CCP-2 mRNA expression and only a slight decrease in cytolytic activity. The expression of CCP-1 and CCP-2 gene products and the induction of MHC-unrestricted cytotoxic activity in anti-CD3-stimulated T cell cultures therefore occur independently of IL-2 synthesis but are regulated by a CsA-sensitive mechanism.

L26 ANSWER 17 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
93:126212 The Genuine Article (R) Number: KP121. COMPARISON OF THE INDUCTION OF ENDOTOXIN TOLERANCE IN ENDOTOXEMIA AND PERITONITIS BY MONOPHOSPHORYL LIPID-A AND LIPOPOLYSACCHARIDE. ASTIZ M E (Reprint); SAHA D C; **BROOKS K**; CARPATI C M; RACKOW E C. ST VINCENTS HOSP & MED CTR, NEW YORK MED COLL, DEPT MED, 153 W 11TH ST, NEW YORK, NY, 10011 Reprint. CIRCULATORY SHOCK (MAR 1993) Vol. 39, No. 3, pp. 194-198. ISSN: 0092-6213. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We compared the induction of endotoxin tolerance with Salmonella minnesota monophosphoryl lipid A (MPL), a nontoxic derivative of lipid A, and S. minnesota endotoxin (LPS) in lethal endotoxemia and peritonitis. Lethal endotoxemia was induced by injecting 750 mug/mouse LPS intravenously. Cecal ligation and perforation was used to induce peritonitis. Tumor necrosis factor (TNF) was measured by immunoassay at 2 hr after lethal endotoxin infusion and 24 hr after peritonitis. A dose of 1.1 mug mouse of MPL or LPS significantly reduced endotoxin mortality from 100% to 50% and 27%, respectively (P < 0.05). The LD50 for a 1.1 mug dose of MPL was 750 mug of LPS and the LD50 for a 1.1 mug dose of LPS was 115 mug of endotoxin (P < 0.05). TNF levels decreased linearly when increasing doses of MPL and LPS were used to induce tolerance. At higher pretreatment

doses of LPS, survival benefits were attenuated despite the reduction in TNF levels. A 25 mug dose of LPS reduced mortality from peritonitis from 93% to 45% ($P < 0.05$). Although MPL reduced short-term mortality, overall mortality was not significantly reduced despite using large doses of MPL. TNF levels peaked at 24 hr and were significantly lower than those following lethal endotoxemia. The induction of endotoxin tolerance by LPS and MPL is dose dependent, and LPS is modestly more effective in inducing endotoxin tolerance than MPL. Both LPS and MPL are significantly less effective in protecting against lethality from peritonitis.

L26 ANSWER 18 OF 37 MEDLINE DUPLICATE 10
94096351 Document Number: 94096351. PubMed ID: 8271238. Inhibition of DNA synthesis and IL-2 bioactivity in MLR by splenic pregnancy-associated natural suppressor cells involves the production of a TGF-beta 1-like molecule and a second distinct inhibitory factor. **Brooks-Kaiser J C**; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Sep) 25 (1) 31-49. Journal code: 8001906. ISSN: 0165-0378. Pub. country: Ireland. Language: English.

AB Natural suppressor cells exhibiting a double-negative, immature T cell phenotype have been identified in maternal spleen during syngeneic murine pregnancy. In the present study, splenic pregnancy-associated natural suppressor (SPANS) cells are shown to express alpha/beta T cell receptors. SPANS cell-mediated inhibition of DNA synthesis by spleen cells responding in mixed lymphocyte reactions (MLR) is associated with a reduction in interleukin (IL)-2 bioactivity beginning after 96 h of culture. Although culture supernatants from suppressed MLR exhibit diminished ability to support the growth of IL-2-dependent CTLL-2 cells, SPANS cells themselves are unable to inhibit IL-2-driven CTLL-2 proliferation, suggesting that SPANS cells down-regulate IL-2 synthesis in MLR. IL-2 utilization in MLR is also inhibited by SPANS cells, since the addition of exogenous IL-2 fails to relieve the inhibitory effect of SPANS cells on lymphoproliferative responses in MLR. Flow cytofluorometric analysis reveals that MLR performed in the presence of SPANS cells contain normal percentages of CD4 and IL-2 receptor-bearing spleen cells. Thus, SPANS cells do not inhibit cellular proliferation in MLR by selectively interfering with clonal expansion of IL-2-producing helper T cells or by down-regulating IL-2 receptor expression. We have determined that SPANS cells inhibit DNA synthesis in MLR via the production of a transforming growth factor (TGF)-beta 1-like suppressor factor, since cellular proliferation in MLR is restored to normal levels in the presence of anti-TGF-beta 1 neutralizing **antibody**. However, IL-2 bioactivity in these cultures remains low in comparison to control MLR, suggesting the presence of a second distinct suppressor factor. Although the identity of this second inhibitory molecule has yet to be determined, neutralizing **antibody** studies have ruled out IL-10.

L26 ANSWER 19 OF 37 MEDLINE DUPLICATE 11
92308750 Document Number: 92308750. PubMed ID: 1535357. Soybean agglutinin-positive natural suppressor cells in mouse bone marrow inhibit interleukin 2 production and utilization in mixed lymphocyte reactions. Hoskin D W; Bowser D A; **Brooks-Kaiser J C**. Department of Microbiology, Dalhousie University, Halifax, Nova Scotia, Canada. JOURNAL OF LEUKOCYTE BIOLOGY, 1992 Jun 51 6 649-56. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Although natural suppressor (NS) cells resident in bone marrow (BM) have been the subject of intensive study, the exact nature and mode of action of these potentially important immunoregulatory cells are still uncertain. Here we show that NS cells with potent inhibitory effects on mixed lymphocyte reactions (MLRs) can be isolated from BM of normal adult mice by agglutination with the plant lectin soybean agglutinin (SBA). Complement-dependent lysis of SBA receptor-bearing BM cells with **antibodies** to asialoGM1, Mac-1, Thy-1.2, J11d.2, and 2G1

phenotypic markers reveals the presence of at least two distinct populations of BM NS cells. Most of the SBA-binding BM cells with NS capacity have the null phenotype and resemble hematopoietic stem cells, and some inhibitory SBA+ BM cells express the 2C1 marker found on pregnancy-associated splenic NS cells and the J11d.2 antigen characteristic of B cells and immature T cells. Results of positive selective experiments confirmed these findings. The mechanism of natural suppression was also studied. Evidence is presented that SBA+ BM cells exert NS activity in MLRs by interfering with the production and utilization of interleukin 2. Indomethacin does not relieve natural suppression associated with SBA+ BM cells, indicating that prostaglandin synthesis is not a requirement for inhibitory function. However, neutralizing **antibodies** to transforming growth factor beta (TGF-beta) partially reverse the suppression mediated by SBA+ BM cells, suggesting that some BM NS cells may act through the release of an immunosuppressive molecule related to TGF beta.

L26 ANSWER 20 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
92:542319 The Genuine Article (R) Number: JM219. CD5 EXPRESSION IS MODULATED AS THE B-CELL MOVES THROUGH THE CELL-CYCLE. **BROOKS K H (Reprint)** ; YOL Y S; PESTKA J J. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES (04 MAY 1992) Vol. 651, pp. 259-260. ISSN: 0077-8923. Pub. country: USA. Language: ENGLISH.

L26 ANSWER 21 OF 37 MEDLINE DUPLICATE 12
92299374 Document Number: 92299374. PubMed ID: 1535063. Reactivity of monoclonal **antibody** 1E5.B5 with a novel phenotypic marker expressed on a murine natural suppressor cell subset. Hoskin D W; **Brooks-Kaiser J C**; Kaiser M; Murgita R A. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia.) HYBRIDOMA, (1992 Apr) 11 (2) 203-15. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.
AB Natural suppressor (NS) cells are antigen-nonspecific, MHC-independent immunoregulatory cells that are typically found in murine bone marrow (BM), newborn (NB) mouse spleen, and in splenic tissue of adult mice during pregnancy and following cyclophosphamide (CY) treatment. There has been a pressing need for the development of NS cell-specific monoclonal **antibodies** (mAb) since NS cells are generally described as null cells which lack the usual phenotypic markers of mature T cells, B cells, and macrophages. Here we present evidence that mAb 1E5.B5, which was raised in rats against murine splenic pregnancy-associated NS (SPANS) cells, recognizes a unique antigenic marker expressed by some, but not all, murine NS cells. In the presence of complement, mAb 1E5.B5 effectively eliminates SPANS activity, and diminishes NS activity of CY-treated spleen cells in mixed lymphocyte reactions (MLR). However, cytotoxic pretreatment with mAb 1E5.B5 had minimal effects on NS activity of BM and NB spleen cells. We also show that pregnancy spleen cells and CY-spleen cells with moderate NS activity in MLR can be positively selected for by "panning" with mAb 1E5.B5. In contrast, only weakly inhibitory cells are isolated from BM and NB spleen by this procedure. Cellular ELISA and flow cytometry confirm that mAb 1E5.B5 has specificity for pregnancy spleen cells and CY-spleen cells, as well as for NB spleen and BM cell preparations. Western blot analysis reveals that mAb 1E5.B5 reacts with a novel 50 kDa NS cell-associated antigen which we have termed NS-1. The NS-1 antigen is not present on other null cells such as natural killer (NK) cells and natural cytotoxic (NC) cells since cytotoxic pretreatment of pregnancy spleen cells with mAb 1E5.B5 does not affect **antibody**-dependent cell-mediated cytotoxicity, NK or NC activity.

L26 ANSWER 22 OF 37 MEDLINE
91339197 Document Number: 91339197. PubMed ID: 1931419. IL-2 and IL-5 both induce mu S and J chain mRNA in a clonal B cell line, but differ in

their cell-cycle dependency for optimal signaling. Takayasu H; **Brooks K H.** (Genetics Program, Michigan State University, East Lansing 48824.) CELLULAR IMMUNOLOGY, (1991 Sep) 136 (2) 472-85. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB We have found that a neoplastic Ly1+ B cell clone (BCL1-3B3) can be stimulated to secrete IgM by a Th1-derived cytokine, IL-2, and/or by a Th2-derived cytokine, IL-5. At suboptimal concentrations these interleukins acted synergistically to enhance IgM secretion. Both IL-2 and IL-5 induced increases in microseconds and J chain mRNA levels. In the presence of both ILs, increases in microseconds and J chain mRNA were additive and paralleled increases in IgM secretion. Using cells synchronized at the G1/S border with excess thymidine or in early G1 using isoleucine-deficient media, IL-2 and IL-5 differed in their cell-cycle dependency for signal transmission. IL-5 appeared to act preferentially in late G1 of the cell cycle. In contrast, IL-2 stimulated S and G2 phase cells slightly more efficiently than cells in G1 of the cell cycle. Furthermore, a twofold increase in high-affinity IL-2R was observed as the cells entered S phase. The results suggest that although IL-2 and IL-5 can independently and additively induce differentiation of the Ly1+ BCL1-3B3 cells, they differ in their point of action during the cell cycle.

L26 ANSWER 23 OF 37 MEDLINE

91007479 Document Number: 91007479. PubMed ID: 2145206. Elevated membrane IgA+ and CD4+ (T helper) populations in murine Peyer's patch and splenic lymphocytes during dietary administration of the trichothecene vomitoxin (deoxynivalenol). Pestka J J; Dong W; Warner R L; Rasooly L; Bondy G S; **Brooks K H.** (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1990 Jun) 28 (6) 409-20. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Recent investigations indicate that dietary exposure to the trichothecene vomitoxin increases total and antigen-specific serum immunoglobulin A (IgA) and glomerular IgA accumulation in mice. In this study, the effects of 25 ppm dietary vomitoxin on the histological and lymphocytic profile of component immune organs in the mucosal lymphocyte migratory pathway were evaluated in the B6C3F1 mouse. Vomitoxin administration resulted in marked stimulation of the size and frequency of germinal centres in Peyer's patches, mesenteric lymph nodes and the spleen. A slight increase in the percentage of B cells in the Peyer's patch was observed, although vomitoxin treatment had no effect on the percentage of B cells in the spleen. The percentage of IgA+ cells in Peyer's patches and spleen were approximately twice that of controls at 4, 8 and 12 wk of vomitoxin exposure whereas the percentage of IgG+ cells decreased in these two organs. Exposure to vomitoxin increased the percentage of T cells in Peyer's patches and the spleen. The percentage of CD4+ cells (T helper subset) increased slightly in Peyer's patches and more markedly (30-50%) in the spleen following vomitoxin treatment. Contrastingly, there was only a slight increase in the percentage of CD8+ cells (T cytotoxic/suppressor subset) in the spleens of vomitoxin-treated mice in comparison with controls, and no effect in Peyer's patches. The relative effects of vomitoxin on these two T cells populations was also reflected in increased CD4+: CD8+ ratios in Peyer's patches and spleen. These results are consistent with the hypothesis that dietary vomitoxin modulates normal regulation of the IgA response at the Peyer's patch level and that this is manifested in an altered lymphocyte distribution pattern in both the mucosal and systemic compartment. Notably increased levels of IgA+ and CD4+ cells are indicative of IgA-producing progenitors and T helper subsets, respectively, that in tandem could favour IgA hyperproduction and elevated IgA in serum.

L26 ANSWER 24 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)

91:258714 The Genuine Article (R) Number: FJ282. CHARACTERIZATION OF A NEOPLASTIC B-CELL CLONE THAT SECRETES IGM IN RESPONSE TO TH2-DERIVED

LYMPHOKINES. **BROOKS K H (Reprint)**; OAKLEY C S; TAKAYASU H. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY 1990; Vol. 4, No. 6, pp. 339-348. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recent advances of T cell cloning have allowed the classification of T helper cells in terms of the lymphokines they secrete. The functional significance of segregating lymphokine production to unique T cell subsets is still being evaluated, but undoubtedly plays a key role in the regulatory mechanisms of the immune system. Initial studies have indicated that the Th1 cells which secrete IL-2 and IFN-gamma may be primarily responsible for augmenting cell-mediated responses, whereas Th2 cells, which release IL-4, IL-5, and IL-6, provide help for humoral responses. However, it is also known that B cells can respond to both IL-2 and IFN-gamma. This raises the question of the homogeneity of B lymphocyte activation requirements. Are all B cells responsive to all of the lymphokines with the end-result of stimulation depending largely on the relative concentrations of the various lymphokines, or are there B cell subsets which only respond to Th1-derived lymphokines and others which respond to Th2-derived lymphokines? Such differential activation requirements might be present to allow these subsets to play unique roles in immunological responses. Since B cell cloning techniques have not yet been developed to obtain a homogenous B cell population for studies of activation requirements, regulation of lymphokine receptors, and regulation of gene expression, we must utilize lymphokine-responsive neoplastic B cells. The vast majority of spontaneous B cell lymphomas appear to belong to a minor B cell subset which expresses the Ly1 marker. This subset is clearly not representative of the majority of splenic B cells. In this report, we have characterized the lymphokine response pattern of Ly1- B cell clones derived from a spontaneous tumor occurring in an AKR mouse.

Neoplastic B cell clones were generated from the 225 lymphoma, which secrete significant levels of IgM upon stimulation with lymphokines produced by type 2 T helper (Th2) cells. The 225 clones expressed a high-density of mIgM, varying densities of mIgD, and were mIgG and Ly1 negative. Th2-derived lymphokines found in D10.G4.1 SN will induce differentiation, as indicated by release of IgM in the culture SN. The 225 cells did not respond to IL-2, IFN-gamma, IL-1, or any combination of these lymphokines. Optimal differentiation occurred only when IL-4, IL-5, and IL-6 were present. The order of differentiative activity of these lymphokines was IL-5 > IL-4 > IL-6. The lack of IL-2 responsiveness in the face of IL-2R-alpha (p55) chain expression was due to the lack of high-affinity IL-2 receptors. In contrast, the IL-2 responsive clone BCL1-3B3 expresses approximately 950 high affinity IL-2R per cell. Thus, the 225-11 clone should provide a useful model system for the evaluation of the regulation of immunoglobulin gene expression mediated by Th2-derived lymphokines.

L26 ANSWER 25 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
91:258713 The Genuine Article (R) Number: FJ252. ADRENOCORTICOTROPIN (ACTH) FUNCTIONS AS A LATE-ACTING B-CELL GROWTH-FACTOR AND SYNERGIZES WITH INTERLEUKIN-5. **BROOKS K H (Reprint)**. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY 1990; Vol. 4, No. 6, pp. 327-337. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In recent years there has been considerable discussion of possible cross-regulatory mechanisms involving the immune system and the neuroendocrine system. Certainly, evidence of hormonal communication between these two systems would provide at least a partial explanation for the many anecdotal observations of physical and mental stress affecting disease course. In previous studies of a neoplastic lymphokine-responsive B cell clone, BCL1-3B3, we noted that these cells produced a lymphokine

which could affect normal B cell growth and viability. Physical characterization of this lymphokine indicated that its molecular weight was identical to that of the neuroendocrine hormone adrenocorticotropin (ACTH). Since Blalock and colleagues had reported the production of ACTH by virally-infected B cells, we have investigated whether ACTH can functionally mimic the BCL1-3B3-derived lymphokine. The neuroendocrine hormone adrenocorticotropin (ACTH) can increase in vitro murine B lymphocyte proliferation when added at physiologically relevant concentrations between 10(-9) to 10 -11 M. ACTH does not mimic the action of any lymphokine known to be required for B cell proliferation such as IL-2, IL-4, or IL-5. ACTH requires the presence of one or more of these known B cell stimulatory factors for its action and the most marked increase in B cell proliferation were noted in assays for IL-5 activity where 10(-10) M ACTH increased thymidine incorporation up to five-fold. Using two-stage assays, we determined that ACTH acts during the latter stages of B cell activation (i.e., 3-4 days after initial stimulation with either the combination of IL-4, GAMIg-Sepharose, and IL-1 or the combination of DxS and IL-5). These data indicate a direct role for a stress-induced neuroendocrine hormone in modulating the course of a humoral immune response.

L26 ANSWER 26 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1987:262595 Document No.: BR33:4491. INTERLEUKIN-2 INDUCES IGM SECRETION IN LYL+ NEOPLASTIC B CELLS BCL-1. **BROOKS K H**; KRAMMER P H; UHR J W; VITETTA E S. DEP. MICROBIOL., UNIV. TEX. HEALTH SCI. CENTER, SOUTHWESTERN MED. SCH., DALLAS, TEX. 75235.. GOLDSTEIN, G., J.-F. BACH AND H. WIGZELL (ED.). UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 41. IMMUNE REGULATION BY CHARACTERIZED POLYPEPTIDES; STEAMBOAT SPRINGS, COLORADO, USA, JANUARY 25-FEBRUARY 1, 1986. XXVI+786P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS. (1987) 0 (0), 305-314. CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2640-7. Language: English.

L26 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2002 ACS
1987:174381 Document No. 106:174381 Interleukin-2 induces IgM secretion in Ly1+ neoplastic B cells (BCL1). **Brooks, Kathryn H.**; Krammer, Peter H.; Uhr, Jonathan W.; Vitetta, Ellen S. (Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA). UCLA Symp. Mol. Cell. Biol., New Ser., Volume Date 1986, 41(Immune Regul. Charact. Polypept.), 305-14 (English) 1987. CODEN: USMBD6. ISSN: 0735-9543.
AB Cells from 2 neoplastic B cell clones have been used to exam. the effect of interleukin-2 (IL-2) on B cell differentiation. Cells from both clones express high levels of secretory IgM but relatively little secretory IgD; however, they differ in their expression of the Ly1 marker. The cells from the Ly1+ BCL1-derived (BALB/c) clone secrete IgM in response to purified and recombinant IL-2. This response can be blocked with monoclonal anti-IL-2 **antibodies**. In contrast, cells from a Ly1- neoplastic B cell clone from AKR mice (AKR-225) do not differentiate in response to IL-2 or IL-2 plus recombinant interferon. The cells from both the BCL1 clone and the AKR-225 clone can differentiate in response to B cell stimulatory factor(s) present in supernatants (SNs) of the alloreactive T cell line, PK 7.1. This PK 7.1 SN lacks significant IL-2 activity but does contain the differentiation factor for IgM. The different activation requirements of these Ly1+ and Ly1- neoplastic B cells is intriguing in light of both the assocn. of normal Ly1+ B cells with autoimmune disease and the prodn. of a B cell growth factor by the Ly1+ BCL1 clone but not the AKR-225 clone.

L26 ANSWER 28 OF 37 MEDLINE DUPLICATE 13
97134946 Document Number: 97134946. PubMed ID: 8945961. Recombinant IL-2 but not recombinant interferon-gamma stimulates both proliferation and IgM secretion in a Ly-1+ clone of neoplastic murine B cells (BCL1 .
Brooks K H; Vitetta E S. JOURNAL OF IMMUNOLOGY, 1996 Nov 15 157

(10) 3205-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have used a lymphokine-responsive clone (3B3) of B leukemia cells (BCL1) to examine the effects of several recombinant and purified lymphokines. Cells from BCL1-3B3 were induced to secrete IgM in the presence of recombinant interleukin 2 (rIL 2, (10 to 50 U/ml)); a concomitant increase in proliferation was observed. Recombinant interferon-gamma (rIFN-gamma) was a potent inhibitor of proliferation. In addition, rIFN-gamma did not induce an increase in IgM secretion and, when added to rIL 2-stimulated BCL1-3B3 cells, completely blocked IgM secretion at a concentration of 10 U/ml. Purified and recombinant IL 1 (rIL 1) had no significant effect on differentiation either alone or in combination with rIL 2 and/or rIFN-gamma. However, rIL 1 was able to synergize with rIL 2 in enhancing the proliferation of BCL1-3B3. The ability of cells to respond to rIL 2 was limited to the in vitro (Ly-1+) clones of BCL1 cells since the in vivo derived (Ly-1-) BCL1 cells did not differentiate in response to IL 2. Consistent with their functional response to rIL 2, cells from the in vitro clone (3B3) are IL 2-receptor-positive (IL-2R+) and the in vivo derived BCL1 cells are IL-2R-. A second set of neoplastic B cell clones derived from the AKR 225 lymphoma did not respond to rIL 2 even though they expressed receptors for IL 2 and could be induced by T cell supernatant to secrete IgM, thus indicating that expression of IL 2R is not the sole requirement for IL 2 responsiveness. The monoclonal anti-IL 2R **antibody** (7D4) mimicked IL 2 in its ability to stimulate differentiation of BCL1-3B3 cells. These data suggest that rIL 2 and the monoclonal anti-IL-2R **antibody** are capable of inducing a differentiative response in the Ly-1+ BCL1-3B3 cells that is functionally equivalent to the response evoked by the previously described lymphokine B cell differentiation factor for IgM (BCDF mu). Thus, two distinct lymphokines appear to be providing a similar signal to a clonal neoplastic B cell population. Furthermore, rIL 2 is capable of providing both a proliferative and a differentiative signal.

L26 ANSWER 29 OF 37 MEDLINE

85081355 Document Number: 85081355. PubMed ID: 3871214. Cell cycle-related expression of the receptor for a B cell differentiation factor. **Brooks K H**; Uhr J W; Vitetta E S. JOURNAL OF IMMUNOLOGY, (1985 Feb) 134 (2) 742-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Cloned, neoplastic B cells (BCL1) have been used to evaluate the expression of the receptor for the B cell differentiation factor, BCDF mu. These cells do not secrete IgM before stimulation with BCDF mu-containing T cell supernatants (SN). By inducing cell cycle synchrony in this homogeneous population, the expression of the BCDF mu receptor could be evaluated as a function of the cell cycle. Responsiveness to BCDF mu-containing SN is maximal when the cells are in S and G2 phases of the cell cycle, and a 2-hr exposure of cells to BCDF mu-containing SN during S/G2 results in optimal IgM secretion 5 days later. Cells in S/G2 are also maximally effective in absorbing BCDF mu activity from SN. These data support the hypothesis that B cells do not respond to differentiative signals until after they are committed to at least one round of cell division.

L26 ANSWER 30 OF 37 EMBASE COPYRIGHT 2012 ELSEVIER SCI. B.V.

94121729 EMBASE Document No.: 1994121729. T cell-derived lymphokines that induced IgM and IgG secretion in activated murine B cells. Vitetta E.S.; **Brooks K.**; Chen Y.-W.; et al.. Department of Microbiology, University of Texas Health Science Center, Dallas, TX 75235, United States. Immunological Reviews VOL. 78 P. 137-157 1994. CODEN: IMREDZ. Pub. Country: Denmark. Language: English.

AB We have defined 2 lymphokine activities, termed BCDF.mu. and BCDF.gamma., which are present in the supernatants of T cell tumors, lines and hybridomas. These lymphokines appear to act directly on activated normal B

cells (or in the case of BCDF.mu., on BCL1 cells as well) to induce the synthesis and secretion of IgM or IgG1, respectively. These lymphokines are different from each other as well as from IL-1, IL-2, IFN.gamma., and conventional TRF. By molecular weight, BCDF.mu. is different from BCGF. The 2 BCDFs appear to bind to 2 different receptors on the cell surface and, thereby, to induce changes in the levels of isotype-specific mRNA and secreted immunoglobulin. The binding of BCDF.mu. to target cells appears to be cell-cycle related (optimal in G2S) and independent of T cells and macrophages. This has not been proven for BCDF.gamma.. It is possible that a subset of cells present in normal B cell populations, but not represented by the cloned BCL1 cells, is needed for BCDF.gamma. activity. Studies from other laboratories describing BCDF.gamma. (Severinson et al. 1982) BCDF.alpha. (Mayer et al. 1982, Kawanishi et al. 1983), and BCDF.epsilon. (Kishimoto & Ishizaka 1973, Hirashima et al. 1981) activities in T cell supernatants suggest that T cell-derived lymphokines may regulate the expression and/or secretion of several classes of immunoglobulin in activated B cells.

L26 ANSWER 31 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1984:44777 Document No.: BR26:44777. LYMPHOKINE INDUCED DIFFERENTIATION OF CLONAL NEOPLASTIC B CELLS. **BROOKS K**; YUAN D; UHR J; KRAMMER P; VITETTA E S. UNIV. TEX. HEALTH SCI. CENT. DALLAS, DALLAS, TEX. 75235.. 67TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, CHICAGO, ILL., USA, APRIL 10-15, 1983. FED PROC. (1983) 42 (5), ABSTRACT 6101. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L26 ANSWER 32 OF 37 MEDLINE DUPLICATE 14
83192467 Document Number: 83192467. PubMed ID: 6601774.
Lymphokine-induced IgM secretion by clones of neoplastic B cells. **Brooks K**; Yuan D; Uhr J W; Krammer P H; Vitetta E S. NATURE, (1983 Apr 28) 302 (5911) 825-6. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The induction of **antibody** secretion by B cells requires T-cell-derived factors1-5. Such factors have been described1,2,6-12 but the precise relationship among these various factors is not clear, and it has been difficult to demonstrate that these factors act directly on the B cell and do not exert their effect via T cells or macrophages. In this report we describe the direct induction of IgM synthesis and secretion in cloned lines of long-term tissue culture adapted neoplastic B cells (BCL1) by T-cell supernatants from phorbol-12-myristate 13-acetate (PMA)-induced EL-4 cells or concanavalin A (Con A)-induced 7.1.1a cells5,9. We have termed this activity BCDFmu (B-cell differentiation factor for IgM). The supernatants containing BCDFmu induce activated and neoplastic B cells to secrete IgM5 and the factor responsible is distinct from BCGF13, interleukin-2 (IL-2)5, the classical T-cell replacing factor (TRF) described by Schimpl and Wecker5, and immune interferon (IFN gamma)5.

L26 ANSWER 33 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15
83152564 EMBASE Document No.: 1983152564. The correlation between the activation state of B cells and their capacity for in vitro propagation of immunologic memory. **Brooks K.H.**; Feldbush T.L.. Dep. Microbiol., Univ. Iowa, Iowa City, IA 52242, United States. Cellular Immunology 76/2 (213-223) 1983.
CODEN: CLIMB9. Pub. Country: United States. Language: English.
AB The B-cell population responsible for in vitro antigen-mediated proliferation and expansion of the memory B-cell population is a large activated blast. Such cells predominate early after antigen priming and can be regenerated by adjuvant Bordetella pertussis stimulation in vivo. Although these cells are proliferating in vivo, additional stimuli are needed for expansion of the memory population in vitro. These triggering requirements include specific antigen (NP-OVA) and the assistance of adherent accessory cells. Although T cells are present in the culture,

their role in the propagation of memory is not completely clear. Using the unrelated antigen, sheep erythrocytes, we have shown that 'bystander' T-cell help can mediate differentiation of these memory B-cell blasts to AFC, but it cannot induce expansion of the memory-cell population. However, the fact that the TI-2 antigen DNP-Ficoll is a relatively ineffective inducer of memory-cell propagation (inducing an expanded response which is less than 10% of that induced by the T-cell-dependent antigen, DNP-OVA) suggests that T cells may be involved, possibly via production of B-cell growth factor. Thus, the minimal requirements for triggering the propagation of B-cell memory include (i) a blastogenic signal which can be mediated by adjuvant, (ii) specific antigen, and (iii) adherent accessory-cell help.

L26 ANSWER 34 OF 37 MEDLINE DUPLICATE 16
81265503 Document Number: 81265503. PubMed ID: 7021678. Generation of **antibody**-mediated regulation during in vitro clonal expansion of memory B lymphocytes. **Brooks K H;** Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 963-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

L26 ANSWER 35 OF 37 MEDLINE
81265502 Document Number: 81265502. PubMed ID: 7021677. In vitro antigen-mediated clonal expansion of memory B lymphocytes. **Brooks K H;** Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 959-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB An in vitro model for the propagation and expansion of the memory B lymphocyte population is described. DNP-BGG immune cells were mixed with OVA immune cells and challenged immediately with DNP-OVA. After the 1st response had begun to wane, the cells were rechallenged with DNP-OVA (day 11 of culture). An average of 13-fold more PFC were observed after delayed challenge (day 11). This expansion in the PFC response was an antigen-dependent process and did not involve recruitment of new memory cells from the virgin lymphocyte pool. The level of expansion of the memory cell pool was also calculated using limiting dilution analysis and was found to fall in a range of 16- to 67-fold increase in precursor frequency. In addition to the expansion of the memory B cell population, we also observed the development of 2 immunoregulatory cycles previously observed only in vivo. First, in the presence of persistent antigen, a cyclical PFC response was seen. Second, after day 10 of culture, optimal PFC numbers were observed only when DNP-lysine was added to the plaque assay. Such hapten-augmentable PFC responses have been reported by other investigators as indicative of anti-idiotypic regulation. This possibility is examined more extensively in the following communication.

L26 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2002 ACS
1982:558292 Document No. 97:158292 Isolation and characterization of an .alpha.1-antitrypsin-related glycoprotein from human liver. Glew, Robert H.; Zidian, J. L.; Chiao, J. P.; Kuhlenschmidt, T.; Iammarino, Richard M.; **Brooks, K. P.** (Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA). Electrophor. '81 (Eighty-One), Proc. Int. Conf., 3rd, 511-21. Editor s): Allen, Robert Chadbourne; Arnaud, Philippe. de Gruyter: Berlin, Fed. Rep. Ger. (English) 1981. CODEN: 48KUAG.

AB A 68,000-dalton glycoprotein which cross-reacts with **antibody** to human plasma .alpha.1-antitrypsin (I) was purified from the 100,000-g supernatant of human liver. This glycoprotein (I-CRM) had 9.5% of the immunoreactivity of I and no antiproteinase activity. Isoelec. focusing resolved I-CRM into 2 fractions which differed in immunoreactivity. Carbohydrate and amino acid analyses were carried out. I-CRM, which differed from I in mol. wt., also differed substantially in CNBr- and chymotrypsin-derived fragments. The basis of the relatedness of plasma I and I-CRM, which represents only .apprx.0.1% of liver protein content, is not known; however, as immunospecificity was the major criteria for

purifn. the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

L26 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
80132519 Document Number: 80132519. PubMed ID: 6153590. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool: effect of time and antigen. **Brooks K H**; Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, 1980 Mar 15; 50 (2): 392-404. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

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NEWS 6 Mar 18 Gene Names now available in BIOSIS
NEWS 7 Mar 22 TOXLIT no longer available
NEWS 8 Mar 22 TROTHERMO no longer available
NEWS 9 Mar 25 US Provisional Priorities searched with P in CA CAplus and USPATFULL
NEWS 10 Mar 25 LIPINSKI/CALC added for property searching in REGISTRY
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NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available
NEWS 19  Jun 03  New e-mail delivery for search results now available
NEWS 20  Jun 10  MEDLINE Reload
NEWS 21  Jun 10  PCTFULL has been reloaded
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=> s l1 and cd23 antibody
L2            11 L1 AND CD23 ANTIBODY
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PROCESSING COMPLETED FOR L2
L3 3 DUP REMOVE L2 (8 DUPLICATES REMOVED)

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L3 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S ; Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody** , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T; Kloetzer W S;** Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E.** (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human PRIMATIZED(R) monoclonal antibodies. PRIMATIZED (R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F ab' 2 of p5E8G1, the F ab' 2 of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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L1          15 CHIMERIC CD23

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L2           6 L1 AND ANTIBOD?

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PROCESSING COMPLETED FOR L2
L3           2 DUP REMOVE L2 (4 DUPLICATES REMOVED)

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L3   ANSWER 1 OF 2     MEDLINE                                  DUPLICATE 1
2000384038  Document Number: 20304490.    PubMed ID: 10845922.   Engagement of
     CD11b and CD11c beta2 integrin by antibodies or soluble CD23
     induces IL-1beta production on primary human monocytes through
     mitogen-activated protein kinase-dependent pathways. Rezzonico R;
     Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and
     Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department
     of Internal Medicine, University Hospital, Geneva, Switzerland..
     rezzonic@unice.it) . BLOOD, (2000 Jun 15) 95 (12) 3868-77.  Journal code:
     7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.
AB   beta2 integrins are involved in the recruitment of leukocytes to
     inflammatory sites and in cellular activation. We demonstrate that
     ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2
     integrins by mAbs or soluble chimeric CD23 (sCD23) on
     human freshly isolated monocytes rapidly stimulates high levels of
     interleukin-1beta production. This induction takes place at the
     transcriptional level and is regulated by members of the mitogen-activated
     protein kinase (MAPK) family. Indeed, stimulation of monocytes through
     engagement of CD11b or CD11c results in the phosphorylation and activation
     of ERK1, ERK2, and p38 SAPK2 MAP kinases. U0126, a potent inhibitor of the
     upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger
     RNA (mRNA) expression in a dose-dependent fashion, showing the implication
     of this pathway in the transcriptional control of IL-1beta production. On
     the other hand, inhibition of p38 by SB215863 indicates that this MAPK is
     involved in the control of IL-1beta production at both transcriptional and
     translational levels. Together these data demonstrate that ligation of
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CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3869-3877.

L3 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:947017 The Genuine Article (R) Number: 146NG. Production of a chimeric form of CD23 that is oligomeric and blocks IgE binding to the Fc epsilon RI. Kelly A E; Chen B H; Woodward E C; Conrad D H (Reprint). VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 980678, MCV STN, RICHMOND, VA 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA 23298. JOURNAL OF IMMUNOLOGY (15 DEC 1998) Vol. 161, No. 12, pp. 6696-6704. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The low affinity receptor for IgE (Fc epsilon RII/CD23) has previously been shown to interact with IgE with a dual affinity. Three chimeric constructs were created containing the lectin domain (amino acids 172-188) or the ''neck'' and lectin domain (amino acids 157-188) attached to subunits of oligomeric proteins. All chimeras were incapable of interacting with IgE with either a high or low affinity, indicating that the alpha-helical stalk of CD23 is important for orienting the lectin heads such that an interaction with IgE can occur. This concept received further support in that a **chimeric CD23** composed of the human CD23 stalk and the mouse CD23 lectin head bound mouse IgE with a dual affinity, but could only bind rat IgE with a low affinity. Effort was next concentrated on a construct consisting of the entire extracellular (EC)region of CD23, A mutation to the first cleavage site of CD23 (C1M) resulted in a more stable molecule as determined by a decrease of soluble CD23 release, A soluble chimeric EC-C1M was prepared by attaching an isoleucine zipper to the amino terminus (1zEC-C1M), The interaction with IgE by 1zEC-C1M was found to be superior to that seen with EC-CD23. The IzEC-C1M could inhibit binding of IgE to both CD23 and the high affinity receptor for IgE, Fc epsilon RI, providing further evidence for a strong interaction with IgE, Fc epsilon RT inhibition (similar to 70-) was seen at equimolar concentrations of IzEC-C1M, implying the effectiveness of this chimera and suggesting its potential therapeutic value.

=> s humanized anti CD23
L4 1 HUMANIZED ANTI CD23

=> d l4 cbib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English . CODEN: PIXXD2. APPLICATION: WO 1999-EP9157 19991201. PRIORITY: GB 1998-26624 19981203.
AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 1.1mM. Thus, NSO cells transfected with an IgG1 **humanized anti -CD23** antibody was cultured for 56 days in a draw and fill

repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in antibody prodn. over the control.

```
=> s monoclonal
L5       727044 MONOCLONAL

=> s l5 and human CD23
   4 FILES SEARCHED...
L6           43 L5 AND HUMAN CD23

=> s l6 and chimeric
L7            7 L6 AND CHIMERIC

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8            3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8   ANSWER 1 OF 3  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946  Document No.: PREV200200370946. Antibodies against the stalk
     region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis.
     Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew;
     Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia
     Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298
     USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239.
     http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of
     Professional Research Scientists on Experimental Biology New Orleans,
     Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB   The stalk region of human CD23 comprising a.a. 48-153
     was expressed in E. coli and purified. In addition a chimeric
     human CD23 was prepared consisting of the extracellular
     region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal
     antisera were produced in rabbits and shown to block binding of IgE to
     CD23 both on cell surfaces as well as the interaction of LZ-CD23 with IgE
     in an ELISA based assay. The antisera was also shown to inhibit IgE
     synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition
     was dose dependent and essentially complete blockage of IgE production was
     seen at a relatively low dose of anti-stalk. FACS analysis using CD23+B
     lymphoblastoid cells indicated little if any endocytosis and/or protection
     from cleavage induced by the anti-stalk. Monoclonal antibodies
     against the human stalk have also been prepared and these are being
     analyzed for the capacity to inhibit IgE binding and IgE synthesis, as
     well as compare their efficacy to the anti-lectin mabs. The results
     indicate that targeting the stalk region is efficacious with respect to
     blocking IgE production.

L8   ANSWER 2 OF 3  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:186685  Document No.: PREV200200186685. Induction of apoptosis by IDEC-152
     (anti-CD23) in lymphoma cells. Pathan, Nuzhat  1 ; Hariharan, Kandasamy
      1 ; Hopkins, Michael; Saven, Alan; Reff, Mitchell  1 ; Hanna, Nabil  1 ;
     Grint, Paul  1 . (1  IDEC Pharmaceuticals, San Diego, CA USA. Blood,
     (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a.
     http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of
     the American Society of Hematology, Part 1 Orlando, Florida, USA December
     7-11, 2001 ISSN: 0006-4971. Language: English.
AB   IDEC-152 is a primatized monoclonal antibody to human
     CD23, the low-affinity receptor for IgE on B cells that has been
     implicated in the regulation of IgE synthesis. In vitro and in vivo data
     have demonstrated that IDEC-152 suppresses IgE synthesis. IDEC-152 is
     currently in clinical trials for use in allergic asthma. CD23 is also
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expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a **chimeric monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab')2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L8 ANSWER 3 OF 3 MEDLINE DUPLICATE 1

2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct **chimeric** macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

=> d his

FILE 'HOME' ENTERED AT 19:24:54 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002

L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBOD?
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23
L7 7 S L6 AND CHIMERIC
L8 3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> s l5 and chimeric CD23
L9 1 L5 AND CHIMERIC CD23

=> d l9 cbib abs

L9 ANSWER 1 OF 1 MEDLINE
2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by antibodies or soluble CD23 induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonic@unice.it) . BLOOD, (2000 Jun 15) 95 (12) 3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger RNA (mRNA) expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3868-3877)

=> s l5 and humanized CD23
L10 0 L5 AND HUMANIZED CD23

=> d his

FILE 'HOME' ENTERED AT 08:24:54 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002
L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBOD?
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23

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L7              7 S L6 AND CHIMERIC
L8              3 DUP REMOVE L7 (4 DUPLICATES REMOVED)
L9              1 S L5 AND CHIMERIC CD23
L10             0 S L5 AND HUMANIZED CD23

=> s l6 and IgE
L11            38 L6 AND IGE

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12            17 DUP REMOVE L11 (21 DUPLICATES REMOVED)

=> d l12 1-17 cbib abs

L12  ANSWER 1 OF 17  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946  Document No.: PREV200200370946. Antibodies against the stalk
     region of huCD23 block binding of IgE and inhibit in vitro
     IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil,
     Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad,
     Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall
     Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16,
     No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual
     Meeting of Professional Research Scientists on Experimental Biology New
     Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language:
     English.
AB   The stalk region of human CD23 comprising a.a. 48-153
     was expressed in E. coli and purified. In addition a chimeric
     human CD23 was prepared consisting of the extracellular
     region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal
     antisera were produced in rabbits and shown to block binding of
     IgE to CD23 both on cell surfaces as well as the interaction of
     LZ-CD23 with IgE in an ELISA based assay. The antisera was also
     shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated
     human PBL model. The inhibition was dose dependent and essentially
     complete blockage of IgE production was seen at a relatively low
     dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells
     indicated little if any endocytosis and/or protection from cleavage
     induced by the anti-stalk. Monoclonal antibodies against the
     human stalk have also been prepared and these are being analyzed for the
     capacity to inhibit IgE binding and IgE synthesis, as
     well as compare their efficacy to the anti-lectin mabs. The results
     indicate that targeting the stalk region is efficacious with respect to
     blocking IgE production.

L12  ANSWER 2 OF 17  CAPLUS  COPYRIGHT 2002 ACS
2001:747174  Document No. 135:287537  Inhibitors for the formation of soluble
     human CD23 and their use in treatment of diseases.
     Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp.
     DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL,
     SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW.
     APPLICATION: EP 2000-107515 20000407.
AB   A pharmaceutical compn. for the treatment or prophylaxis of disorders is
     described in which the overprodn. of sCD23 is implicated. This compn.
     comprises an inhibitor for the formation of human sol. CD23 which
     inhibitor decreases or blocks selectively the activity of the
     metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in
     human B-cell lines. Also described is a pharmaceutical compn. wherein the
     inhibitor for the formation of human sol. CD23 is a monoclonal
     or polyclonal antibody directed against the metalloprotease ADAM9 or
     wherein the inhibitor is an antisense oligonucleotide which is specific
     for c-myc. Such a pharmaceutical compn. may be used in a method for
     selectively inhibiting the formation of ADAM9 as well as the formation of
     sCD23. It is a suitable medicament against inflammatory disorders,
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autoimmune diseases and allergy.

L12 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:186685 Document No.: PREV200200186685. Induction of apoptosis by IDEC-152 (anti-CD23) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized **monoclonal** antibody to **human CD23**, the low-affinity receptor for **IgE** on B cells that has been implicated in the regulation of **IgE** synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses **IgE** synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric **monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L12 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-**human CD23 monoclonal** antibodies. Reff, Mitchell E. (1); Kloetzer, William S.; Nakamura, Takehiko. (1) San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011139 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-**human CD23 monoclonal** antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L12 ANSWER 5 OF 17 MEDLINE DUPLICATE 1
2001151173 Document Number: 21151173. PubMed ID: 11694997. In vitro **IgE** inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.

INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for **IgE** (FcvarepsilonRII), is involved in regulation of **IgE** synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of **IgE** complexes to CD23 positive cells and also inhibited the production of **IgE** in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited **IgE** production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in **IgE** inhibition. An F(ab')(2) of p5E8G1 did not inhibit **IgE** production but did interfere with **IgE** inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits **IgE** production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit **IgE** production. These data imply that the mechanism by which anti-CD23 antibodies inhibit **IgE** production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit **IgE** production.

L12 ANSWER 6 OF 17 MEDLINE

2000150237 Document Number: 20150237. PubMed ID: 10684962. Characterization of novel FcepsilonRII/CD23 isoforms lacking the transmembrane (TM) segment in human cell lines. Yoshikawa T; Matsui M; Gon Y; Yoshioka T; Hirama M; Lynch R G; Naito K; Yodoi J. (Institute for Virus Research, Kyoto University, 53 Kawahara-cho, Sakyo-ku, Kyoto, Japan.) MOLECULAR IMMUNOLOGY, (1999 Dec) 36 (18) 1223-33. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Human FcepsilonRII/CD23 is an approximately 45 kDa type II transmembrane glycoprotein belonging to the C-type animal-lectin family, and has two isoforms (a and b) that only differ in their intracytoplasmic tails. We previously found that in several human and mouse cell lines there were two additional CD23 transcripts (a' and b') lacking the exon 3 that encodes the entire transmembrane segment and a part of cytoplasmic tails. In this study, we analyzed the putative CD23a' and CD23b' products at protein levels and characterized with rabbit polyclonal antibodies against novel amino-acid sequences of the putative CD23a' and CD23b' molecules (anti-CD23a' Ab, anti-CD23b' Ab). Western blots in COS cells transfected with CD23a' or CD23b' cDNA as well as in vitro translation assays showed that the a' and b' CD23 transcripts were translated to about 40 kDa molecules. These 40 kDa molecules were also recognized by a polyclonal antibody against 25 kDa soluble fragment of **human CD23**. We also found that human cells having mRNAs for CD23a' and CD23b' expressed protein products recognized specifically by anti-CD23a' or anti-CD23b' Ab, respectively. In addition, the CD23a' and CD23b' molecules in transfected COS cells were resistant to Endo H (f) and PNGase F, although these truncated forms as well as the membrane-associated forms had an asparagine residue responsible for the N-linked glycosylation. Taken together, our results show that the a' and b' CD23 transcripts are expressed and translated in human lymphoid cells and that their translated products are retained in the cytoplasm where they might play an unique regulatory role in the expression of the full-length CD23 on the cell surface.

L12 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
1999:275763 Document No.: PREV199900275763. In vitro suppression of **IgE** synthesis by a primatized **monoclonal** antibody (mab) against **human CD23** antigen. Li, Yan-Ping; Kloetzer, William; Nakamura, Takehiko (1); Chen, Agnes; Brams, Peter; Hariharan, Kandasamy; Chamat, Soulaima; Cao, Xianjun; LaBarre, Michael; Chinn, Paul; Morena, Ron; Shestowsky, William; Hanna, Nabil; Reff, Mitchell. (1) Seikagaku Corp., Tokyo Japan. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A989. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April 17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L12 ANSWER 8 OF 17 MEDLINE DUPLICATE 3
1999111232 Document Number: 99111232. PubMed ID: 9893160. Upregulated surface expression of intracellularly sequestered Igepsilon receptors (FcepsilonRII/CD23) following activation in human peripheral blood eosinophils. Sano H; Munoz N M; Sano A; Zhu X; Herrnreiter A; Choi J; Leff A R. (Department of Medicine, Section of Pulmonary and Critical Care Medicine.) PROCEEDINGS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1999 Jan-Feb) 111 (1) 82-91. Journal code: 9514310. ISSN: 1081-650X. Pub. country: United States. Language: English.

AB We investigated the regulation, secretion, and surface expression of the low-affinity FcepsilonRII receptor (CD23) in eosinophils isolated from human blood using multiple **monoclonal** antibodies (mAbs) directed at different epitopes of **human CD23**. Substantial surface expression of CD23 was not demonstrated in the resting state. Mean fluorescence intensity (MFI) measured by flow cytometry was 7. 1 +/- 0.8 for 9P25 mAb (p = NS) and 15.7 +/- 3.8 for BU38 mAb (p <. 04) versus 5.3 +/- 1.0 for IgG1 isotype control Ab. By contrast, MFI using BU38 mAb was 154 +/- 18 for JY-B lymphocytes (p <.0001 versus eosinophils). Despite weak surface expression, eosinophil permeabilization demonstrated substantial intracellular expression of CD23; MFI was 33.6 +/- 5.2 for 9P25 mAb versus 4.4 +/- 0.43 for IgG control (p <.001). Western blot analysis using both positive and negative controls demonstrated immunological identity with CD23 on JY-B lymphocytes. Activation of eosinophils caused rapid translocation of CD23 to the surface membrane (160 +/- 33 MFI; p <. 005), which was maximal within 30 sec. Secretory CD23 was detected within the perfusate also at 30 sec and was fully reinternalized at 10 min. This is the first demonstration of the presence of intracellular CD23 in human eosinophils. Our data indicate that eosinophils rarely express CD23 on their surface but are capable of transient high-level expression and secretion with rapid reuptake of intracellular stores of CD23.

L12 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human CD23 monoclonal** antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, CW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English . CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB **Monoclonal** antibodies which specifically bind **human CD23**, the low affinity receptor for **IgE** FcεRII/CD23 , and contain either a human gamma-1 or human gamma-3 const. domain, are

disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L12 ANSWER 10 OF 17 MEDLINE DUPLICATE 4
97351082 Document Number: 97351082. PubMed ID: 9207459. Inhibition of apoptosis in a human pre-B-cell line by CD23 is mediated via a novel receptor. White L J; Ozanne B W; Graber P; Aubry J P; Bonnefoy J Y; Cushley W. (Institute of Biomedical & Life Sciences, University of Glasgow, Scotland, UK.) BLOOD, (1997 Jul 1; 90 (1) 234-43. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB **Human CD23** is a 45-kD type II membrane glycoprotein, which functions as a low-affinity receptor for **IgE** and as a ligand for the CD21 and CD11b/CD11c differentiation antigens. CD23 is released from the surface of cells as soluble fragments, and a 25-kD species of soluble CD23 (sCD23) appears to act as a multifunctional cytokine. In this report, sCD23 is shown to sustain the growth of low cell density cultures of a human pre-B-acute lymphocytic leukemia cell line, SMS-SB: no other cytokine tested was able to induce this effect. Flow cytometric analysis indicates that sCD23 acts to prevent apoptosis of SMS-SB cells. SMS-SB cells cultured at low cell density possess low levels of bcl-2 protein. Addition of sCD23 to cells at low cell density maintained bcl-2 expression at levels equivalent to those observed in SMS-SB cells cultured at higher cell densities. No CD23 mRNA was found in SMS-SB cells, ruling out an autocrine function for CD23 in this cell line model. Although SMS-SB cells do not express the known receptors for CD23, namely CD21, CD11b-CD18, or CD11c-CD18, the cells specifically bind CD23-containing liposomes, but not glycophorin-containing liposomes. Binding of CD23-containing liposomes is inhibited by anti-CD23 but not by anti-CD21 or anti-CD11b/c **monoclonal** antibodies. The data show that sCD23 prevents apoptosis of the SMS-SB cell line by acting through a novel receptor.

L12 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of **IgE** production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect Immunofluorescence of **monoclonal** antibodies, for **IgE**, IL-4 with ELISA, for IL-2 with F12-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with anti **human CD23** McAb. The mechanism of T cells and cytokines in the regulation of **IgE** production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of **IgE**, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant **IgE** difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of **IgE** antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L12 ANSWER 12 OF 17 MEDLINE DUPLICATE 5
94009242 Document Number: 94009242. PubMed ID: 7691616. CD21 expressed on basophilic cells is involved in histamine release triggered by CD23 and anti-CD21 antibodies. Bacon K; Gauchat J F; Aubry J P; Pochon S; Graber P; Henchoz S; Bonnefoy J Y. Glaxo Institute for Molecular Biology, Plan-Les-Ouates, Geneva, Switzerland. : EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Oct) 23 (10) 2721-4. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Recombinant full-length **human CD23** incorporated into fluorescent liposomes was used to detect a ligand for CD23 on the basophilic leukemia cell line, KU 812. Based on our recent finding that CD23 interacts with CD21 on subsets of B and T cells, we investigated if the same ligand was involved on KU 812 cells. An anti-CD21 **monoclonal** antibody (mAb) BU-33, was able to totally block CD23-liposome binding to KU 812 cells. Moreover, KU 812 cells express CD21 mRNA and have a cell surface molecule that reacts with anti-CD21 mAb. The CD23/CD21 interaction was not merely physical but was also associated with an increase in histamine release by KU 812 cells. Both recombinant soluble CD23 and an anti-CD21 mAb-mediated effect on histamine release was not restricted to and anti-CD21 mAb-mediated effect on histamine release was not restricted to the leukemic cell line, but was also observed with normal human blood basophils. These data demonstrate that CD21 is expressed on basophilic cells and that CD21 controls histamine production upon ligand-induced stimulation (CD23 or anti-CD21 mAb).

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
1993:470048 Document No. 119:70048 The mechanisms of **IgE** uptake by human alveolar macrophages and a human B-lymphoblastoid cell line (Wil-2wt). Richardson, D. R.; Cameron, K.; Robinson, B.; Turner, K. J. (Dep. Microbiol., Univ. West. Australia, Nedlands, Australia). Immunology, 79(2), 305-11 (English) 1993. CODEN: IMMUAM. ISSN: 0019-2805.

AB Human alveolar macrophages (HAM) internalized more **IgE** (81-) than human Wil-2wt B-lymphoblastoid cells (28-) suggesting a difference in the metabolic processing of the specific **IgE** receptor (CD23) or, alternatively, the presence of another functionally distinct receptor. The mannose receptor (MR), demonstrated to be present on the AM, may fulfill this role as **IgE** is heavily mannosylated and binds to a greater extent to Con A (which has specificity for oligomannose oligosaccharide chains) than other antibody isotypes. The hypothesis of a second **IgE** receptor was tested using mannan which is a competitive inhibitor of ligand binding to the MR and mannosylated bovine serum albumin (MBSA) which binds with avidity to the MR. Mannan (0.1 mg/mL) decreased internalized MBSA uptake in the HAM at 37.degree. suggesting the presence of the specific MR. In contrast, Wil-2wt cells did not bind MBSA. Mannan also reduced **IgE** uptake in the HAM at 37.degree. but had no effect on **IgE** uptake by Wil-2wt cells. Anti-CD23 **monoclonal** antibody (mAb) 135 also partially reduced membrane **IgE** uptake in HAM while completely inhibiting it by Wil-2wt cells. However, there did not appear to be competition for binding sites between **IgE** and MBSA in HAM. If only CD23 is involved in **IgE** uptake by HAM its function appears to be different to that in Wil-2wt cells. Definite involvement of the MR in **IgE** uptake will require further investigation as it may have an important role in allergic states.

L12 ANSWER 14 OF 17 MEDLINE DUPLICATE 6
93149182 Document Number: 93149182. PubMed ID: 1385115. Cytokine effects of CD23 are mediated by an epitope distinct from the **IgE** binding site. Mossalayi M D; Arock M; Delespesse G; Hofstetter H; Bettler B; Dalloul A H; Kilchherr E; Quaas F; Lebre P; Sarfati M. Groupe d'Immuno-Hematologie Moleculaire, CHU Pitie-Salpetriere, Paris, France. EMBO JOURNAL, 1992 Dec 11 12 4823-8. Journal code: 8208664. ISSN:

0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **Human CD23** and its soluble forms (sCD23) display various biological activities, in addition to their **IgE** binding function (**IgE**/BF). The **IgE** binding domain was recently mapped to residues between Cys163 and Cys282 but its involvement in **IgE**-independent, CD23 functions remains unknown. In order to clarify this point, a series of N-terminal, C-terminal and internal deletion mutants of CD23 or sCD23 were expressed in CHO cells and tested for their ability (i) to bind to **IgE**, (ii) to induce colony formation by human myeloid precursor cells, (iii) to promote mature T cell marker expression by early prothymocytes, and (iv) to regulate **IgE** synthesis. The present study indicates that cytokine activities require the presence of Cys288, while this amino acid is not necessary for **IgE**/BF. Blocking experiments using various conformation-sensitive **monoclonal** antibodies further suggest that active epitope(s) of CD23 in cytokine assays is(are) distinct from those involved in **IgE**/BF.

L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS

1992:253891 Document No. 116:253891 Heterogeneity among Epstein-Barr virus-seropositive donors in the generation of immunoblastic B-cell lymphomas in SCID mice receiving human peripheral blood leukocyte grafts. Picchio, Gaston R.; Kobayashi, Ryo; Kirven, Marybeth; Baird, Stephen M.; Kipps, Thomas J.; Mosier, Donald E. (Div. Immunol., Med. Biol. Inst., La Jolla, CA, 92037, USA). Cancer Res., 52(9), 2468-77 (English) 1992. CODEN: CNREA8. ISSN: 0008-5472.

AB Epstein-Barr virus (EBV) is assocd. with B-cell malignancy in immunosuppressed humans and SCID mice receiving human peripheral blood leukocyte grafts (hu-PBL-SCID). Here, the process of lymphoma development was further characterized in hu-PBL-SCID mice. EBV-seropos. donors differ markedly in the capacity of their PBL to give rise to immunoblastic lymphomas in SCID mice; some donors (high incidence) generated tumors rapidly in all hu-PBL-SCID mice, other donors (intermediate-low incidence) gave rise to sporadic tumors after a longer latent period (>10 wk), and some donors failed to produce tumors. B-cell lymphomas arising from high incidence donors were multiclonal in origin, and EBV replication was detected in all tumors. Tumors derived from intermediate-low incidence donors were **monoclonal** or oligoclonal and often had no evidence of viral replication. All tumors, regardless of the donor, resembled EBV-transformed lymphoblastoid cell lines in surface phenotype but differed from lymphoblastoid cell lines by having less Epstein-Barr nuclear antigen 2 and CD23 expression. The variable patterns of lymphomagenesis seen among different EBV-seropos. donors may be explained by lower levels of specific immunity to EBV in high incidence donors, permitting activation of EBV replication and potential transformation of secondary B-cell targets. In addn. there may be differences in the transforming potential of EBV infecting different donors. The use of the hu-PBL-SCID model may help predict patients at high risk for posttransplant or AIDS-assocd. lymphomas.

L12 ANSWER 16 OF 17 MEDLINE DUPLICATE 7

92364541 Document Number: 92364541. PubMed ID: 1386872. Demonstration of a second ligand for the low affinity receptor for immunoglobulin E CD23 using recombinant CD23 reconstituted into fluorescent liposomes. Pochon S; Graber P; Yeager M; Jansen K; Bernard A R; Aubry J P; Bonnefoy J Y. Glaxo Institute for Molecular Biology, Plan-Les-Ouates, Geneva, Switzerland. JOURNAL OF EXPERIMENTAL MEDICINE, 1992 Aug 1 176 2 399-97. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Recombinant full-length **human CD23** has been incorporated into fluorescent liposomes to demonstrate the existence of a ligand for CD23 that is different from the previously known ligand, immunoglobulin E **IgE** . The novel ligand for CD23 is expressed

on subsets of normal T cells and B cells as well as on some myeloma cell lines. The interaction of full-length CD23 with its ligand is specifically inhibited by anti-CD23 **monoclonal** antibodies and by **IgE**, and it is Ca2+ dependent. Moreover, tunicamycin treatment of a CD23-binding cell line, RPMI 8226, significantly reduced the binding of CD23 incorporated into fluorescent liposomes, and a sugar, fucose-1-phosphate, was found to inhibit CD23-liposome binding to RPMI 8226 cells, suggesting the contribution of sugar structures on the CD23 ligand. In addition, CD23-transfected COS cells were shown to form specific conjugates with the cell line RPMI 8226. These data demonstrate that CD23 interacts with a ligand, which is different from **IgE**, and that CD23 can be considered as a new surface adhesion molecule involved in cell-cell interactions.

L12 ANSWER 17 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
91341164 EMBASE Document No.: 1991341164. Expression of human recombinant CD23 in insect cells. Jansen K.U.; Shields J.; Gordon J.; Cairns J.; Graber P.; Bonnefoy J.-Y.. Glaxo Institute for Molecular Biology S.A. 46 route des Acacias, 1211 Geneva 24, Switzerland. Journal of Receptor Research 11/1-4 (507-520) 1991.
ISSN: 0197-5110. CODEN: JRERDM. Pub. Country: United States. Language: English. Summary Language: English.

AB **Human CD23** (low affinity receptor for **IgE**) has been expressed in insect cells (Sf9) using the baculovirus expression system and the baculovirus transfer vector pAc373. Insect cells infected with a recombinant baculovirus coding for CD23 synthesized a polypeptide not found in wild-type infected insect cells that had antigenic properties similar to natural CD23 produced in RPMI 8866 cells. Surface expression of recombinant CD23 was demonstrated by its ability to bind **IgE**. Recombinant CD23 expressed in insect cells had a slightly lower molecular weight (43 kDa) than that of natural CD23 (45 kDa) from RPMI 8866 cells as detected by SDS-PAGE followed by Western-blotting. Affinity-purified recombinant CD23 from infected insect cells showed B-cell growth promoting activity. These observations demonstrate for the first time that biologically active recombinant CD23 can be produced by the baculovirus expression system, thus providing a useful source of recombinant material to elucidate the biological functions of CD23.

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L2             6 S L1 AND ANTIBOD?
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L4             1 S HUMANIZED ANTI CD23
L5        727044 S MONOCLONAL
L6            43 S L5 AND HUMAN CD23
L7             7 S L6 AND CHIMERIC
L8             3 DUP REMOVE L7  4 DUPLICATES REMOVED
L9             1 S L5 AND CHIMERIC CD23
L10            3 S L5 AND HUMANIZED CD23
L11           39 S L6 AND IGE
L12           17 DUP REMOVE L11  21 DUPLICATES REMOVED
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L14 3 DUP REMOVE L13 (4 DUPLICATES REMOVED)

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L14 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-**human** **CD23 monoclonal** antibodies. Reff, Mitchell E. (1); Kloetzer, William S.; Nakamura, Takehiko. 1 San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-**human CD23 monoclonal** antibodies containing **human gamma 1** constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L14 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro **IgE** inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for **IgE** (FcvarepsilonRII), is involved in regulation of **IgE** synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of **IgE** complexes to CD23 positive cells and also inhibited the production of **IgE** in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing **human gamma 1** constant region, inhibited **IgE** production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in **IgE** inhibition. An F(ab')(2) of p5E8G1 did not inhibit **IgE** production but did interfere with **IgE** inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits **IgE** production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit **IgE** production. These data imply that the mechanism by which anti-CD23 antibodies inhibit **IgE** production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit **IgE** production.

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
1999:634934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human** **CD23 monoclonal** antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9937788 A1 19990729, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,

BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB **Monoclonal** antibodies which specifically bind **human CD23**, the low affinity receptor for **IgE** FceRII/CD23, and contain either a **human gamma-1** or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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=> s IgE and allery
L15           9 IGE AND ALLERY

=> s l15 and anti human CD23
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L20        2077 L19 AND ANTIBODY

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L21           2 L20 AND HUMAN CD23

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L22  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2002 ACS
2001:747174   Document No. 135:287537  Inhibitors for the formation of soluble
      human CD23 and their use in treatment of
      diseases.  Frey, Juergen (Germany).  Eur. Pat. Appl. EP 1142910 A1
      20011010, 29 pp.  DESIGNATED STATES: R:  AT, BE, CH, DE, DK, ES, FR, GB,
      GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO.  (English).
      CODEN: EPXXDW.  APPLICATION: EP 2000-107515 20000407.
AB    A pharmaceutical compn. for the treatment or prophylaxis of
      disorders is described in which the overprodn. of sCD23 is implicated.
      This compn. comprises an inhibitor for the formation of human sol. CD23
      which inhibitor decreases or blocks selectively the activity of the
      metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in
      human B-cell lines.  Also described is a pharmaceutical compn. wherein the
      inhibitor for the formation of human sol. CD23 is a monoclonal or
      polyclonal antibody directed against the metalloprotease ADAM9
      or wherein the inhibitor is an antisense oligonucleotide which is specific
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for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and **allergy**.

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human** **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind **human** **CD23**, the low affinity receptor for **IgE** (FceRII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the **treatment** or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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L23 42683 (REFF M?/AU OR KLOETZER W?/AU OR NAKAMURA T?/AU)

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L24 11 L23 AND CD23 ANTIBODY

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L25 3 DUP REMOVE L24 (8 DUPLICATES REMOVED)

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L25 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells. Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S ; Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody**, p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L25 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
20000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T**; **Kloetzer W S**; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E**. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L25 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors "Molly" and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, Ml+Neomycin

phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
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NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment

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L2          150 L1 AND INHIBIT IGE

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L3            0 L2 AND "ANTI HUMAN CD23"

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L4   ANSWER 1 OF 1  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946  Document No.: PREV200200370946. Antibodies against the stalk
     region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis.
     Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew;
     Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia
     Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298
     USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239.
     http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of
     Professional Research Scientists on Experimental Biology New Orleans,
     Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB   The stalk region of human CD23 comprising a.a. 48-153 was expressed in E.
     coli and purified. In addition a chimeric human
     CD23 was prepared consisting of the extracellular region of CD23
     linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were
     produced in rabbits and shown to block binding of IgE to CD23 both on cell
     surfaces as well as the interaction of LZ-CD23 with IgE in an ELISA based
     assay. The antisera was also shown to inhibit IgE synthesis in an
     anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose
     dependent and essentially complete blockage of IgE production was seen at
     a relatively low dose of anti-stalk. FACS analysis using CD23+B
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lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. Monoclonal antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

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L5 0 L2 AND CD23 ANTIBODY

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L6 2321935 ANTIBOD?

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L9 1 L8 AND PRIMATE

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L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FceRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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L10 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2012:220424 Document No. 156:246419 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2012028812 A2 20120301, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MA, MD, MX, NO,

NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L10 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2002036168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M.. M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized** monoclonal Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L10 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L10 ANSWER 4 OF 12 MEDLINE DUPLICATE 1

2001262398 Document Number: 21203341. PubMed ID: 11307028.
Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcepsilonRI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized** anti-IgE mAb Hu-901 can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.

AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "**humanized**" monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L11 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:961519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Ieboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000079979 A1 20001228, 31 pp.
DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ,

EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.

AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (IgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized** anti-**CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, **humanized** IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 10^6 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L10 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko

(Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FceRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L10 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L10 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of

monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L10 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS
1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Frendscho, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940118.
AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s monkey anti human CD23
L11 0 MONKEY ANTI HUMAN CD23

=> d his

(FILE 'HOME' ENTERED AT 13:19:26 ON 05 JUL 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON 05 JUL 2002
L1 10122901 S METHOD
L2 150 S L1 AND INHIBIT IGE
L3 0 S L2 AND "ANTI HUMAN CD23"
L4 1 S CHIMERIC HUMAN CD23
L5 0 S L2 AND CD23 ANTIBODY
L6 2321935 S ANTIBOD?
L7 3178 S L6 AND CD23
L8 16 S L7 AND HUMANIZED
L9 1 S L8 AND PRIMATE
L10 12 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L11 0 S MONKEY ANTI HUMAN CD23

=> s l7 and human gamma 1 constant region
4 FILES SEARCHED...
L12 5 L7 AND HUMAN GAMMA 1 CONSTANT REGION

=> dup remove l12
PROCESSING COMPLETED FOR L12
L13 1 DUP REMOVE L12 (4 DUPLICATES REMOVED)

=> d l13 cbib abs

L13 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-**CD23** monoclonal **antibodies** is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan. INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000 Feb 22 (2) 181-91. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
AB **CD23**, the low affinity receptor for IgE FcvarepsilonRII , is

involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal **antibodies** to human **CD23** were generated from cynomolgus macaques immunized with purified soluble **CD23** (sCD23). Four of the five primate **antibodies** blocked the binding of IgE complexes to **CD23** positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate **antibodies** were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal **antibodies**. PRIMATIZED(R) p5E8G1, containing **human gamma 1 constant region**, inhibited IgE production in vitro as efficiently as the parent primate **antibody**, but the human gamma 4 constant version, PRIMATIZED(R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal **antibody** MHM6 recognizes human **CD23** at a different epitope than primate **antibody** 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of **CD23** to an IgG receptor. These data also imply that neither bivalent cross-linking of **CD23** alone or inhibition of **CD23** binding to its natural ligands is sufficient to inhibit IgE production.

```
=> s primatized CD23
L14           0 PRIMATIZED CD23

=> d his

     (FILE 'HOME' ENTERED AT 13:19:26 ON 05 JUL 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 13:19:38 ON
     05 JUL 2002
L1      10122901 S METHOD
L2           150 S L1 AND INHIBIT IGE
L3             0 S L2 AND "ANTI HUMAN CD23"
L4             1 S CHIMERIC HUMAN CD23
L5             0 S L2 AND CD23 ANTIBODY
L6       2321935 S ANTIBOD?
L7          3178 S L6 AND CD23
L8            16 S L7 AND HUMANIZED
L9             1 S L8 AND PRIMATE
L10           12 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L11            0 S MONKEY ANTI HUMAN CD23
L12            5 S L7 AND HUMAN GAMMA 1 CONSTANT REGION
L13            1 DUP REMOVE L12 (4 DUPLICATES REMOVED)
L14            0 S PRIMATIZED CD23

=> s l7 and human IgG1 Fc
L15            3 L7 AND HUMAN IGG1 FC

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16            1 DUP REMOVE L15 (2 DUPLICATES REMOVED)

=> d l16 qbib abs

L16 ANSWER 1 OF 1      MEDLINE                                  DUPLICATE 1
92325512 Document Number: 92325512.     PubMed ID: 1378175.   Soluble forms of
     CD23 inhibit biologic responses of human B cells. Fanslow W C; Anderson D
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M; Grabstein K H; Clark E A; Cosman D; Armitage R J. (Department of Immunology, Immunex Research and Development Corporation, Seattle, WA 98101.) JOURNAL OF IMMUNOLOGY, (1992 Jul 15) 149 (2) 655-60. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have expressed the CD40 surface Ag as both a soluble 28-kDa molecule and a 57-kDa Fc fusion protein containing the **human IgG1 Fc** region. Soluble CD40 and the Fc fusion protein inhibited the proliferative response of anti-IgM-activated human B cells to the CD40 mAb G28-5. Similarly, G28-5- and IL-4-induced IgE secretion from PBMC depleted of T cells was effectively blocked by both forms of soluble CD40. Although the soluble constructs of CD40 had only a minimal inhibitory effect on IL-4-mediated proliferation of anti-IgM-activated B cells, IL-4-induced soluble **CD23** shedding from both PBMC and T cells depleted of PBMC, and IgE secretion from PBMC, were significantly reduced in a concentration-dependent manner when soluble CD40 was present in the culture. The data presented demonstrate that both soluble forms of the CD40 molecule are biologically active, and suggest that the ligand for CD40 is inducible in IL-4-stimulated cultures and that it mediates both shedding of sCD23 and IgE secretion.

=> s l7 and humanized
L17 16 L7 AND HUMANIZED

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 12 DUP REMOVE L17 (4 DUPLICATES REMOVED)

=> d l18 1-12 cbib abs

L18 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS
2002:220424 Document No. 136:246408 Combination therapy for treatment of autoimmune diseases using B cell depleting/immunoregulatory **antibody** combination.. Hanna, Nabil (Idec Pharmaceuticals, USA). PCT Int. Appl. WO 2002022212 A2 20020321, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, EE, ES, FI, GB, GE, GM, HU, ID, IL, IN, KP, KR, LK, LR, MN, MW, MX, NO, NZ, PL, PT, RO, RU; RW: AT, BE, CG, CH, CI, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US29026 20010918. PRIORITY: US 2000-PV257147 20001222.

AB The present invention concerns treatment of autoimmune diseases with the combination of an immunoregulatory **antibody**, e.g. and anti-B7.1 or anti-B7.2 or anti-CD40L **antibody** and at least one B cell **antibody**, such as CD19, CD20, CD22, **CD23**, or CD37, wherein such **antibodies** may be administered sep., or in combination, and in either, over prolonged periods of time.

L18 ANSWER 2 OF 12 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
2002036168 EMBASE Anti-IgE-**antibodies** in the treatment of allergic diseases. Soler M., M. Soler, Pulmonary Division, University Hospital, CH-4031 Basel, Switzerland. msoler@uhbs.ch. Revue Francaise d'Allergologie et d'Immunologie Clinique 42/1 (45-49) 2002.
Refs: 25.
ISSN: 0335-7457. CODEN: RFAIBB. Pub. Country: France. Language: English. Summary Language: English; French.

AB In an established type-I allergy, the IgE molecule is the main mechanism by which the organism specifically recognizes the inhaled allergen. When the IgE molecule is bound to its high-affinity receptor on the surface of a mast cell, it also provides the link between the allergen and the immediate mast cell activation and mediator release, which are the central steps in the type-I immune response. The **humanized** monoclonal

Anti-IgE **antibody** omalizumab binds to free IgE molecules in the serum and thereby prevents them from attaching to the high affinity IgE-receptors on the mast cell surface. This treatment, when given on a regular basis, is able to block the antigen-induced tissue responses in the bronchi and in the skin. In large scale clinical trials it proved to be effective in controlling allergic asthma, preventing exacerbations and reducing the need for inhaled and/or systemic steroid treatment. In more than 1500 patients treated for at least 1 year, the compound showed excellent safety and tolerability. This new treatment may have an important place in the future treatment of moderate to severe allergic asthma, especially if the patient needs a complex treatment that still allows for recurrent exacerbations. A major advantage of this treatment lies in its ability to control nasal and eye symptoms of the allergic disease at the same time. .COPYRGT. 2002 Editions scientifiques et medicales Elsevier SAS.

L18 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:747174 Document No. 135:287537 Inhibitors for the formation of soluble human **CD23** and their use in treatment of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the treatment or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. **CD23** which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. **CD23** is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and allergy.

L18 ANSWER 4 OF 12 MEDLINE DUPLICATE 1
2001262398 Document Number: 21203341. PubMed ID: 11307028.
Humanized anti-IgE mAb Hu-901 prevents the activation of allergen-specific T cells. van Neerven R J; van Roomen C P; Thomas W R; de Boer M; Knol E F; Davis F M. (Tanox Pharma BV, Amsterdam, The Netherlands.. joostvanneerven@tanox.nl) . INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (2001 Jan-Mar) 124 (1-3) 400-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: As a result of the very efficient capture of allergens by IgE that focuses to **CD23** on B cells or FcepsilonRI on dendritic cells, allergen-specific T cells can be activated after exposure to very low levels of allergens. This IgE-mediated allergen presentation is 100- to 1,000-fold more efficient than fluid phase endocytosis. The aim of the present study was to determine whether **humanized** anti-IgE mAb Hu-901 can prevent the activation of allergen-specific T cells by inhibiting IgE-mediated allergen presentation. METHODS: A house dust mite major allergen Der p 1-specific T cell line was generated from an allergic asthma patient, and a model was set up to show IgE-facilitated allergen presentation via **CD23** on EBV-transformed B cells. In addition, experiments were performed by FACS analysis, detecting the presence of IgE-allergen complexes bound to EBV-B cells by polyclonal FITC-labeled anti-IgE antisera. RESULTS: The anti-IgE mAb Hu-901 inhibited proliferation of allergen-specific T cells at low allergen concentrations. Inhibition was dose-dependent. This effect could be explained by Hu-901 inhibition of binding of allergen-IgE complexes to **CD23** expressed on EBV-transformed B lymphocytes. CONCLUSIONS: These data

clearly indicate that anti-IgE **antibodies** for the treatment of allergy exert their effect not only by inhibiting mast cell/basophil degranulation, but also by preventing T cell activation, which possibly explains the effect of anti-IgE treatment on late-phase reactions noted in clinical studies.
Copyright 2001 S. Karger AG, Basel

L18 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
2001:361001 Document No. 136:52380 Allergen, IgE and mast-cell-directed therapies: An overview. Larche, Mark; Kay, A. Barry (Department of Allergy and Clinical Immunology, National Heart and Lung Institute, Imperial College School of Medicine, London, UK). Progress in Respiratory Research, 31(New Drugs for Asthma, Allergy and COPD), 182-185 (English) 2001. CODEN: PRRRAE. ISSN: 1422-2140. Publisher: S. Karger AG.
AB A review. In addn. to traditional drug development strategies, a no. of current approaches focus on modulation of the immune response to allergens or the allergens themselves. Disease-modulating specific immunotherapy has been used for many years and has been shown to be efficacious, although this form of treatment is slow and carries the risk of systemic adverse reactions. The identification of naturally occurring allergen isoforms of the native protein which do not bind IgE has led to modification of a no. of allergens by site-directed mutagenesis. Such proteins have a reduced or absent interaction with IgE while retaining much of their ability to stimulate T cells. The improved safety profile of such mols. may result in larger, more efficacious doses of protein being given with improved safety. Fragments of allergen mols., such as peptides, are also under development, employing a similar rationale of destroying IgE binding epitopes while retaining T cell determinants. Neutralization of specific mols. in the inflammatory cascade is currently being addressed with "**humanized**" monoclonal **antibodies** and sol. receptors/receptor antagonists, directed towards IgE, cytokines such as IL-4 and IL-5, and cell surface mols. such as **CD23**.

L18 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:861519 Document No. 134:16552 Treating allergic diseases with immunotherapy and IgE antagonists. Deboer, Mark; Van Neerven, Joost (Tanox, Inc., USA). PCT Int. Appl. WO 2000072879 A1 20001207, 31 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13446 20000516. PRIORITY: US 1999-PV136068 19990526.
AB The invention relates to methods of treating allergic diseases with a combination of immunotherapy and IgE antagonists by inhibiting the binding of IgE mols. to IgE receptors (IgE Fc receptor type I and **CD23**), expressed by cells of the immune system. In one embodiment, anti-IgE **antibodies** are used and allergy inhibitors. Disclosed is a mouse (TES-C21) and chimeric mouse-human (TESC-2) anti-IgE **antibody** and fragments as allergy inhibitors.

L18 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan. Glaxo Group Limited, UK. PCT Int. Appl. WO 2000039298 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG,

CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28624 19981223.

AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 0.1mM. Thus, NSO cells transfected with an IgG1 **humanized** anti-**CD23 antibody** was cultured for 56 days in a draw and fill repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in **antibody** prodn. over the control.

L18 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

1999:736930 Document No. 131:350265 **Antibodies** to **CD23**. Bonnefoy, Jean-Yves Marcel Paul; Crowe, Scott James; Ellis, Jonathan Henry; Rapson, Nicholas Timothy; Shearin, Jean (Glaxo Group Limited, UK). PCT Int. Appl. WO 9958679 A1 19991118, 81 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1434 19990507. PRIORITY: GB 1998-9839 19980509.

AB The authors disclose the prepn. and characterization of murine monoclonal and **humanized antibodies** which bind to the **CD23** (Fc.epsilon.RII receptor) antigen. In one example, **humanized** IgG1, with mutations to eliminate C1q and Fc binding, was shown to bind to **CD23** with assocn. rates of the order of 1.5-1.85 x 106 M-1 s-1 and to not exhibit complement activation or ADCC. The authors suggest these **antibodies** may find use in the treatment of autoimmune and inflammatory disorders.

L18 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-human **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal **antibodies** which specifically bind human **CD23**, the low affinity receptor for IgE (FceRII/**CD23**), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L18 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380154 Document No. 125:56235 Binding agents for treatment of inflammatory, autoimmune or allergic diseases. Bonnefoy, Jean-Yves Marcel Paul; Lecoanet-Henchoz, Sybille (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612742 A1 19960502, 51 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE,

KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4110 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to CD11b, CD11c, CD21, **CD23**, a 70 to 85 KDa protein expressed on endothelial cells or a 115 KDa protein expressed on endothelial cells, can be useful in the treatment of inflammatory, autoimmune or allergic disease. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were **CD23** -liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, competition of **CD23**-liposomes with Epstein-Barr virus, interferon .alpha., C3 peptide and C3d,g, etc.

L18 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

1996:380155 Document No. 125:31943 Binding agents to **CD23**. Bonnefoy, Jean-Yves Marcel Paul (Glaxo Group Limited, UK). PCT Int. Appl. WO 9612741 A1 19960502, 50 pp. DESIGNATED STATES: W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-EP4109 19951020. PRIORITY: GB 1994-21463 19941025; GB 1995-12480 19950620; GB 1995-13415 19950630.

AB Binding agents to **CD23** useful in the treatment of inflammatory, autoimmune or allergic diseases. The binding agent is a **humanized antibody** or fragment. Demonstrated in examples were preventative treatment of mice against arthritis using monoclonal anti-**CD23** **antibody**, **CD23**-liposomes bind to CD14+ mononuclear cells and .alpha. chain of CD11b/CD18 and CD11c/CD18 recombinant transfectants, anti-CD11b and anti-CD11c monoclonal **antibodies** decrease **CD23**-liposome binding to activated blood monocytes, increases of monocyte nitrate prodn., oxidative burst and cytokine prodn. by binding recombinant **CD23** to CD11b and CD11c, etc.

L18 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS

1995:789548 Document No. 123:196599 IgE antagonists for treatment of parasitic infection. Amiri, Payman; Haak-Fredscho, Mary; Jardieu, Paula M. (Genentech, Inc., USA). PCT Int. Appl. WO 9519181 A1 19950720, 28 pp. DESIGNATED STATES: W: JP, MX; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US87 19950105. PRIORITY: US 1994-184083 19940118.

AB This invention concerns a method for the prevention and treatment of parasitic infection by administering an IgE antagonist. The invention further concerns pharmaceutical compns. and bispecific mols. useful in such method. In example, anti-IgE monoclonal **antibody** reduced serum IgE, serum interleukin 4 and interferon .gamma., number of adult worms and eggs, and hepatosplenomegaly following Schistosoma mansoni infection in mice. The IgE antagonist also reduced the enhancement of **CD23** expression in splenic lymphoid cells.

=> s anti human CD23
L19 9 ANTI HUMAN CD23

=> dup remove L19

PROCESSING COMPLETED FOR L19
L20 5 DUP REMOVE L19 (3 DUPLICATES REMOVED)

=> d 120 1-5 cbib abs

L20 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 **anti-human CD23** monoclonal antibodies. Reff, Mitchell E. (1); Kloetzer, William S.; Nakamura, Takehiko. (1) San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB **Anti-human CD23** monoclonal antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced IgE production by B-cells significantly greater than antibodies containing other constant domains.

L20 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. Reff, Mitchell R.; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and **Anti-human CD23** antibody and immunoadhesin in Desmond marked CHO cells was achieved.

L20 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:315723 Gamma-1 and gamma-3 **anti-human CD23** monoclonal antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO

9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB Monoclonal antibodies which specifically bind human CD23, the low affinity receptor for IgE (FceRII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced IgE expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced IgE prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L20 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of IgE production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect Immunofluorescence of monoclonal antibodies, for IgE, IL-4 with ELISA, for IL-2 with F12-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with **anti human CD23** McAb. The mechanism of T cells and cytokines in the regulation of IgE production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of IgE, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant IgE difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of IgE antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L20 ANSWER 5 OF 5 MEDLINE DUPLICATE 1
91010830 Document Number: 91010830. PubMed ID: 1698879. A bioassay for the measurement of human interleukin-4. Siegel J P; Mostowski H S. (Division of Cytokine Biology, Center for Biologics Evaluation and Research, FDA, Bethesda, MD.) JOURNAL OF IMMUNOLOGICAL METHODS, (1990 Sep 14) 132 (2) 287-95. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB We have developed a bioassay for human IL-4 based upon its ability to upregulate CD23 (low affinity IgE receptor) expression. Ramos, a B lymphocyte line derived from a Burkitt lymphoma, was repetitively subcloned yielding a clone, Ramos.G6.C10, which is several fold more sensitive to this effect of IL-4. In microtiter plates cells were cultured for 48 h in the presence of dilutions of recombinant human IL-4 or samples, and then stained with murine **anti-human CD23** and goat anti-mouse IgG-FITC. IL-4 induced an eight-fold increase (6[illegible] channel shift) in fluorescence intensity as measured by flow cytometry. Significant effects were observed at an IL-4 concentration of 5[illegible] pg/ml and increased with concentrations up to 8[illegible] pg/ml. Inter- and intra-assay coefficients of variation were 1[illegible] and 1[illegible] respectively. The

bioassay showed good specificity for IL-4; however, tumor necrosis factors alpha and beta, at optimal concentrations, gave readings barely at the threshold of detection.

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=> s (rempel f?/au or brooks k?/au)
L21       1255 (REMPEL F?/AU OR BROOKS K?/AU)

=> s l21 and anti CD23
L22          0 L21 AND ANTI CD23

=> s l21 and antibody
L23         83 L21 AND ANTIBODY

=> s l23 and CD23
L24          0 L23 AND CD23

=> s l23 and IgE
L25          1 L23 AND IGE

=> d l25 cbib abs

L25  ANSWER 1 OF 1     MEDLINE
95048595  Document Number: 95048595.    PubMed ID: 7525472.   B-1 cells in
      systemic autoimmune responses: IgM+, Fc epsilon Rdull B cells are lost
      during chronic graft-versus-host disease but not in murine AIDS or
      collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M;
      Brooks K H. (Department of Microbiology, Michigan State
      University, East Lansing 48824. ) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug)
      23 (4-5) 293-311.  Journal code: 8504629. ISSN: 0882-0139. Pub. country:
      United States. Language: English.
AB    The potential role of B-1 cells (i.e. the CD5+ B cell and "sister" B cell
      subsets) in autoimmunity is controversial. CD5+ B cells have been shown to
      secrete antibodies of similar specificity as those found in many
      systemic autoimmune diseases; in addition, increases in CD5+ B cell
      frequency have been reported in patients suffering from rheumatoid
      arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent
      diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are
      due to expansion of B-1 lineage cells in the human or due to
      activation-induced expression of CD5 by conventional B cells is unclear.
      In the present study, we used three murine models of systemic
      autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic
      graft-versus-host disease (cGvHD), and collagen-induced arthritis (CIA) to
      determine whether increases in B-1 cell frequency are universally seen in
      models of autoimmunity which are mechanistically distinct. In contrast to
      the aforementioned human systemic autoimmune diseases which exhibit an
      increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined
      in all three murine models of systemic autoimmune disease. Even though
      there was a decrease in the frequency of CD5+ B cells there was no change
      in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B
      cell frequency was due to increases in either T cells, conventional Fc
      epsilon R+ B cells, or both. The only actual decline in a B cell subset
      was the loss of IgM+, Fc epsilon Rdull cells in both the spleen and
      peritoneal cavity of mice undergoing a chronic graft-versus-host reaction.
      Therefore, our data suggests that expansion of the B-1 subset does not
      occur as a general feature of murine systemic autoimmune disease. These
      observations, consistent with previous studies of Ig gene usage in
      autoreactive antibodies, support the view that expansion and
      differentiation of the CD5+ B cell subset is not a central event leading
      to autoantibody production.

=> dup remove l23
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PROCESSING COMPLETED FOR L23
L26 37 DUP REMOVE L23 (46 DUPLICATES REMOVED)

=> d l26 1-37 cbib abs

L26 ANSWER 1 OF 37 MEDLINE DUPLICATE 1
2002200719 Document Number: 21904109. PubMed ID: 11906504. Increased expression of the neuronal glutamate transporter (EAAT3/EAAC1) in hippocampal and neocortical epilepsy. Crino Peter B; Jin Hong; Shumate Melissa D; Robinson Michael B; Coulter Douglas A; **Brooks-Kayal Amy R.** (PENN Epilepsy Center, Department of Neurology, University of Pennsylvania, Philadelphia, Pennsylvania, USA.) EPILEPSIA, (2002 Mar) 43 (3) 211-8. Journal code: 2983306R. ISSN: 0013-9580. Pub. country: United States. Language: English.

AB PURPOSE: To define the changes in gene and protein expression of the neuronal glutamate transporter (EAAT3/EAAC1) in a rat model of temporal lobe epilepsy as well as in human hippocampal and neocortical epilepsy. METHODS: The expression of EAAT3/EAAC1 mRNA was measured by reverse Northern blotting in single dissociated hippocampal dentate granule cells from rats with pilocarpine-induced temporal lobe epilepsy (TLE) and age-matched controls, in dentate granule cells from hippocampal surgical specimens from patients with TLE, and in dysplastic neurons microdissected from human focal cortical dysplasia specimens. Immunolabeling of rat and human hippocampi and cortical dysplasia tissue with EAAT3/EAAC1 **antibodies** served to corroborate the mRNA expression analysis. RESULTS: The expression of EAAT3/EAAC1 mRNA was increased by nearly threefold in dentate granule cells from rats with spontaneous seizures compared with dentate granule cells from control rats. EAAT3/EAAC1 mRNA levels also were high in human dentate granule cells from patients with TLE and were significantly elevated in dysplastic neurons in cortical dysplasia compared with non-dysplastic neurons from postmortem control tissue. No difference in expression of another glutamate transporter, EAAT2/GLT-1, was observed. Immunolabeling demonstrated that EAAT3/EAAC1 protein expression was enhanced in dentate granule cells from both rats and humans with TLE as well as in dysplastic neurons from human cortical dysplasia tissue. CONCLUSIONS: Elevations of EAAT3/EAAC1 mRNA and protein levels are present in neurons from hippocampus and neocortex in both rats and humans with epilepsy. Upregulation of EAAT3/EAAC1 in hippocampal and neocortical epilepsy may be an important modulator of extracellular glutamate concentrations and may occur as a response to recurrent seizures in these cell types.

L26 ANSWER 2 OF 37 MEDLINE DUPLICATE 2
2001183114 Document Number: 21128425. PubMed ID: 11233905. Improved flow cytometric detection of HLA alloantibodies using pronase: potential implications in renal transplantation. Vaidya S; Cooper T Y; Avandsalehi J; Barnes T; **Brooks K**; Hymel P; Noor M; Sellers R; Thomas A; Stewart D; Daller J; Fish J C; Gugliuzza K K; Bray R A. (Department of Pathology, University of Texas Medical Branch, Galveston 77555-0178, USA.) TRANSPLANTATION, (2001 Feb 15) 71 (3) 422-8. Journal code: 0132144. ISSN: 0041-1337. Pub. country: United States. Language: English.

AB BACKGROUND: Flow cytomeric crossmatch (FCXM) has grown in popularity and has become the "standard of practice" in many programs. Although FCXM is the most sensitive method for detecting alloantibody, the B cell FCXM has been problematic. Difficulties with the B cell FCXMs have been centered around high nonspecific fluorescence background owing to Fc-receptors present on the B cells and autoantibodies. To improve the specificity and sensitivity of the B cell FCXM, we utilized the proteolytic enzyme pronase to remove Fc receptors from lymphocytes before their use in FCXM. METHODS: Lymphocytes isolated from peripheral blood, spleen, or lymph nodes were treated with pronase and then used in a three-color FCXM. A total of 167 T- and B cell FCXMs using pronase-treated and untreated cells were performed. Testing used serial dilutions of HLA allosera (22 class I and 6

class II), with the titer of each **antibody** at one dilution past the titer at which the complement-mediated cytotoxicity anti-human globulin crossmatch became negative. RESULTS: After pronase treatment, the actual channel values of the negative control in both T cell and B cell FCXMs declined from 78+/-10 to 57+/-4 (P<0.05) and 107+/-11 to 49+/-3 (P<0.00001), respectively. Pronase treatment resulted in improved sensitivity of the T and B cell FCXM in detecting class I **antibody** by 20- and 80-, respectively. In no instance was a false-positive reaction observed. In this study, pronase treatment improved the specificity of B cell FCXM for detecting class II **antibodies** from 75- to 100- (P=0.03). In no instance was a false-negative reaction recorded. Lastly, on the basis of these observations we re-evaluated three primary transplant recipients who lost their allografts because of accelerated rejection. One of the patients was transplanted across negative T and B cell FCXM, whereas the other two patients were transplanted across a positive T cell, but negative B cell, FCXM. After pronase treatment, T and B cell FCXMs of each patient became strongly positive, and donor-specific anti-HLA class I **antibody** was identi. fied in each case. CONCLUSION: Utilization of pronase-treated lymphocytes improves both the sensitivity and specificity of the FCXM.

L26 ANSWER 3 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:495043 Document No.: PREV200000495164. Influenza vaccine may induce auto-reactive IgG **antibodies** detectable in flow cytometry crossmatches. Cooper, T. Y. (1); Avandsalehi, J. (1); Hymel, P. (1); Barnes, T. (1); Thomas, A. (1); Sellers, R. (1); **Brooks, K. (1)**; Noor, M. (1); Qiu, S. M. (1); Gugliuzza, K. (1); Daller, J. (1); Vaidya, S. (1). (1) Departments of Pathology and Surgery, University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (2000) Vol. 61, No. Supplement 2, pp. S80. print. Meeting Info.: 26th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Lake Buena Vista, Florida, USA October 10-14, 2000 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English. Summary Language: English.

L26 ANSWER 4 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1999:472830 Document No.: PREV199900472830. High background fluorescence may contribute to false negative B lymphocyte flow cytometry crossmatches. Cooper, T. (1); Hymel, P. (1); Thomas, A. (1); **Brooks, K. (1)**; Avandsalehi, J. (1); Stewart, D.; Bray, R.; Vaidya, S. (1). (1) Department of Pathology, The University of Texas Medical Branch, Galveston, TX USA. Human Immunology, (1999) Vol. 60, No. SUPPL. 2, pp. S140. Meeting Info.: 25th Annual Meeting of the American Society for Histocompatibility and Immunogenetics New Orleans, Louisiana, USA October 20-24, 1999 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 5 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:483339 The Genuine Article (R) Number: ZU842. Modulation of IL-1 beta, IL-6 and TNF-alpha secretion and mRNA expression by the trichothecene vomitoxin in the RAW 264.7 murine macrophage cell line. Wong S S; Zhou H R; MarinMartinez M L; **Brooks K**; Pestka J J (Reprint). MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT BLDG, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL CTR FOOD SAFETY & TOXICOL, E LANSING, MI 48824. FOOD AND CHEMICAL TOXICOLOGY MAY 1998 Vol. 36, No. 5, pp. 409-419. Publisher: PERGAMON-ELSEVIER SCIENCE LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0278-6915. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Oral exposure of mice to vomitoxin (VT) has been previously shown to

enhance gene expression of several cytokines associated with macrophage activation. Here, the effects of exposure to VT in vitro on cytokine secretion and mRNA expression were determined in the murine macrophage cell line RAW 264.7. Enzyme-linked immunosorbent assay (ELISA) of supernatants revealed that significant increases in secreted tumour necrosis factor alpha (TNF-alpha) were observed 2 days after exposure to VT at. 100 ng/ml and 250 ng/ml, both with and without lipopolysaccharide (LPS) activation. While VT did not affect IL-6 secretion in the absence of LPS, significantly increased IL-6 production was observed in culture supernatants after 1, 2 and 5 days of exposure to VT at 250 ng/ml in the presence of LPS. Soluble IL-1 beta was not detected in control or VT-treated cell cultures with or without LPS activation. Immunochemical staining of intracellular cytokines in conjunction with flow cytometric analysis was used to detect the effects of VT on the percentage of positive cells and output per cell. The percentage of cells that produced intracellular TNF-alpha were significantly increased at 100 and 250 ng/ml VT with and without LPS whereas increased IL-6 output per cell was observed at 100 and 250 ng/mI VT with LPS. To assess the effects of VT on cytokine mRNA expression, RAW 264.7 cells were analysed semi-quantitatively using reverse transcription-polymerase chain reaction(RT-PCR) in conjunction with Southern hybridization analysis. Elevated TNF-alpha mRNA was observed at 100 and 250 ng VT/ml at 6 and 24 hr in the absence of LPS. With the addition of LPS, superinduction of TNF-alpha was not observed in the presence of VT. Increased IL-1 beta and IL-6 mRNAs were observed at 100 and 250 ng VT/ml at 24 hr in the presence of LPS. These results demonstrated that VT could superinduce both cytokine secretion and mRNA levels in macrophage cultures.

L26 ANSWER 6 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:182785 The Genuine Article (R) Number: YZ186. Role of macrophages in elevated IgA and IL-6 production by Peyer's patch cultures following acute oral vomitoxin exposure. Yan D (Reprint); Zhou H R; **Brooks K H;** Pestka J J. MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI 48824 (Reprint); MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, INST ENVIRONM TOXICOL, E LANSING, MI 48824; MICHIGAN STATE UNIV, NATL FOOD SAFETY & TOXICOL, E LANSING, MI 48824. TOXICOLOGY AND APPLIED PHARMACOLOGY (FEB 1998) Vol. 148, No. 2, pp. 261-273. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS. 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. ISSN: 0041-008X. Pub. country: USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Oral vomitoxin (VT) exposure in mice results in elevated cytokine gene expression, increased production of IgA, and IgA nephropathy, To determine the potential role of macrophages (M phi) in these effects, an ex vivo model was devised whereby Peyer's patch (PP) and spleen cells were prepared from mice 2 h after oral exposure to 0 or 25 mg/kg body wt VT, cultured, and then evaluated for IgA and cytokine IL-6 production, Both PP and, to a lesser extent, spleen cells from treatment mice produced more IgA over a 7-day period than did corresponding control cells when cultured without a costimulus or in the presence of either phorbol myristate acetate plus ionomycin (PMA + ION) or lipopolysaccharide (LPS); IgA elevation was most marked in LPS-treated cultures. The VT effect was completely ablated in PP cultures that were depleted of M phi but not in M phi-depleted spleen cultures, VT exposure similarly increased production of IL-6, an important helper factor for IgA secretion, in LPS-stimulated PP and spleen cell cultures, IL-6 production was also ablated by M phi depletion, A potential costimulatory role for M phi was further suggested because both IgA and IL-6 production increased when M phi-depleted PP cells from VT-treated animals were cocultured with peritoneal M phi from VT-treated animals, Similar effects were observed when an analogous ex vivo approach was used with purified PP B cells and peritoneal M phi. PP B cells from control animals also secreted elevated levels of IgA when

cocultured with splenic CD4(+) cells from VT-treated animals, thus confirming previous studies showing that T cell help also contributes to increased IgA production, Potential roles for soluble mediators and cell contact in this process were suggested when IgA production was measured in cultures of PP cells separated from VT-treated M phi by a semipermeable membrane, Taken together, these and previous results suggest that M phi may play a key mechanistic role in elevated IgA production and IgA nephropathy in VT-exposed mice. (C) 1998 Academic Press.

L26 ANSWER 7 OF 37 MEDLINE DUPLICATE 3
1998432619 Document Number: 98432619. PubMed ID: 9761452. The glutamate transporter, GLT-1, is expressed in cultured hippocampal neurons. **Brooks-Kayal A R**; Munir M; Jin H; Robinson M B. (Department of Neurology, Children's Hospital of Philadelphia, Children's Seashore House, University of Pennsylvania, 19104, USA.. kayal@email.chop.edu) . NEUROCHEMISTRY INTERNATIONAL, (1998 Aug) 33 (2) 95-100. Journal code: 8006959. ISSN: 0197-0186. Pub. country: ENGLAND: United Kingdom. Language: English.

AB There are multiple subtypes of Na+-dependent glutamate transporters. Several studies suggest that EAAC1 and EAAT4 are expressed in neurons, while GLT-1 and GLAST expression is thought to be restricted to glia. In the present study, expression of GLT-1 and EAAC1 was examined in cultured rat hippocampal neurons using single cell mRNA amplification and immunocytochemistry with subtype specific **antibodies**. GLT-1 and EAAC1 mRNAs were observed in all neurons examined. Neuronal phenotype was confirmed in these cells by expression of neurofilament (NF-L) mRNA and absence of glial fibrillary acidic protein (GFAP) mRNA. EAAC1 immunoreactivity was observed in essentially all cells which expressed neuron specific enolase (NSE) and GLT-1 immunoreactivity was detected in the majority (approximately 90%) of NSE-positive cells. Consistent with the glial expression of GLT-1, GLT-1 immunoreactivity was also observed in NSE-negative cells. These studies provide evidence that GLT-1 expression is not intrinsically restricted to glial cells, but can occur in neurons under certain circumstances.

L26 ANSWER 8 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:470990 Document No.: PREV199800470990. Impact of positive flow crossmatches on primary renal transplants. Cooper, Todd; Vaidya, Smita; Asfour, M. Ayman; Avandsalehi, Jeanne; Barnes, Titus; **Brooks, Karl** ; Lopez, Sheila; Partlow, David; Sellers, Racheal; Thomas, Alice. Univ. Tex. Med. Branch, Galveston, TX USA. Human Immunology, (1998) Vol. 59, No. SUPPL. 1, pp. 7. Meeting Info.: 24th Annual Meeting of the American Society for Histocompatibility and Immunogenetics Vancouver, British Columbia, Canada October 10-15, 1998 American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 9 OF 37 MEDLINE DUPLICATE 4
97418734 Document Number: 97418734. PubMed ID: 9274810. Potential role for IL-5 and IL-6 in enhanced IgA secretion by Peyer's patch cells isolated from mice acutely exposed to vomitoxin. Yan D; Zhou H R; **Brooks K H**; Pestka J J. (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824, USA.) TOXICOLOGY, (1997 Sep 26) 122 (1-2) 145-58. Journal code: 0361055. ISSN: 0300-483X. Pub. country: Ireland. Language: English.

AB Dietary exposure to vomitoxin (VT) results in hyperelevated serum IgA and IgA nephropathy in mice. To assess the possible role of cytokines in this IgA dysregulation, the effects of a single oral exposure in B6C3F1 male mice to 0, 5 or 25 mg/kg BW VT on production of IgA and cytokines in Peyer's patch (PP) and spleen cell cultures were evaluated. IgA levels were increased significantly in PP cell cultures prepared from mice at 2 or 24 h after oral exposure to VT and subsequently stimulated with phorbol myristate acetate (PMA) and ionomycin (ION) or with lipopolysaccharide (LPS). Significant effects on IgA production were not observed in spleen

cell cultures. Since cytokines such as IL-2, IL-4, IL-5 and IL-6 have been shown to promote IgA production, the effect of the same VT exposure regimen on secretion of these mediators was determined in PP and spleen cultures. Supernatant IL-2 and IL-4 levels were unaffected by the prior treatment of animals with VT. In contrast, IL-5 levels were increased significantly in 7-day PP cell cultures obtained 2 h after VT exposure both with and without PMA + ION exposure but not in other cultures. IL-6 levels were increased significantly in LPS-treated cultures prepared from PP at 2 and 24 h following exposure to VT. IL-6 levels were also elevated significantly in both PMA + ION or LPS treated cultures from spleen isolated at 2 h but not 24 h post VT exposure. To determine whether IL-5 or IL-6 play a role in IgA hyperelevation in vitro, PP and spleen cells from mice obtained 2 h after exposure to 25 mg/kg VT were cultured in the presence of neutralizing cytokine **antibodies** (Abs) and IgA production was monitored. Consistent with IL-5's previously documented role in IgA production, anti-IL-5 decreased IgA levels to background in cultures of both control and VT-exposed PP or spleen cells in the presence of either PMA + ION or LPS. Similar results were seen with addition of anti-IL-6. IgA levels were decreased to a lesser extent in PP cells cultured with LPS and in spleen cells cultured with PMA + ION from VT-exposed mice to which anti-IL-2 Ab was added. Thus, the potential for enhanced IgA production exists in lymphocytes as early as 2 h and as late as 24 h after a single oral exposure to VT and this may be related to the increased capacity to secrete helper cytokines of T cell and macrophage origin. Taken together, the results suggest that the superinduction of cytokine expression may, in part, be responsible for upregulation of IgA secretion in mice exposed orally to VT.

L26 ANSWER 10 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1998:62941 Document No.: PREV199800062941. Acute rejection of a living related kidney associated with positive T-cell flow cytometry crossmatch. Cooper, T. Y.; Sellers, R. B.; Asfour, M. A.; Lopez, S. B.; Moller-Nichols, M.; Barnes, T. H.; **Brooks, K.**; Partlow, D.; Avandsalehi, J.; Thomas, A.; Vaidya, S.. Dep. Pathol., Univ. Texas Med. Branch, Galveston, TX USA. Human Immunology, (1997) Vol. 55, No. SUPPL. 1, pp. 75. Meeting Info.: 23rd Annual Meeting of the American Society for Histocompatibility and Immunogenetics Atlanta, Georgia, USA October 14-19, 1997 The American Society for Histocompatibility and Immunogenetics. ISSN: 0198-8859. Language: English.

L26 ANSWER 11 OF 37 MEDLINE DUPLICATE 5
96022850 Document Number: 96022850. PubMed ID: 7549055. Clinical importance of pre-morteum blood lymphocytes in cadaver donor tissue typing. Vaidya S; Orchard P; Schroeder N; Haneke R; **Brooks K**; Thomas A; Corba A; Asfour A; Fish J C. (Department of Pathology, University of Texas Medical Branch, Galveston 77555 0546, U.S.A.) CLINICAL TRANSPLANTATION, (1995 Jun) 9 (3 Pt 1) 165-70. Journal code: 8710240. ISSN: 0902-0063. Pub. country: Denmark. Language: English.
AB We have refined our immunomagnetic bead (IM bead) procedures to isolate pure and viable lymphocyte subpopulation from pre-morteum (PM) blood for cadaver donor HLA typing, preliminary and final crossmatches (XMs). The results of 1220 XMs were compared using T/B lymphocytes isolated either from PM blood or spleen/lymphnode (SPLN) tissue. IM bead technique was used to isolate T/B cells from PM blood and nylon wool column (NWC) technique was used to isolate T/B cells from SPLN. When we compared the outcome of 800 T-cell crossmatches using T cells from PM blood or SPLN of 5 separate cadaver donors, NWC TXMs tended to be more falsenegative for high PRA (> 10%, total 500 XMs) as well as low PRA (< 10%, total 300 XMs) did not reach statistical significance. In contrast, NW BXM (420 B XM) were found to be far more false negative than IM bead BXM regardless of the PRA of the patients. In order to ensure that NWC BXMs were indeed false negative, 23 sera with known anti-DR **antibodies** were BXMed where antigen-specific B cells were isolated by both the techniques. Our

results showed that IM bead BXM identified the DR specificities greater than 90- of the time, the titers of ab specificities were stronger (1:8). In comparison, NWB cell XMs were weak (titers 1:2), and the false negative rate for some ab was as high as 73-. Using IM bead and NWC techniques we compared our turnaround time (TAT) for cadaver donor typing, preliminary and final XMs.(ABSTRACT TRUNCATED AT 250 WORDS)

L26 ANSWER 12 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
94251909 EMBASE Document No.: 1994251909. In vitro effects of vomitoxin (deoxynivalenol) on T-cell interleukin production and IgA secretion. Warner R.L.; **Brooks K.**; Pestka J.J.. Dept. of Food Sci./Human Nutrition, 234 G.M. Trout Bldg., Michigan State University,East Lansing, MI 48824-1224, United States. Food and Chemical Toxicology 32/7 (617-625) 1994.
ISSN: 0278-6915. CODEN: FCTOD7. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The exposure of lymphocyte cultures to vomitoxin was used to determine possible mechanism by which this naturally occurring toxin induces serum immunoglobulin A (IgA) elevation and IgA nephropathy in the mouse. Vomitoxin exposure within the range of 10 to 1000 ng/ml inhibited DNA synthesis, protein synthesis as well as IgA, IgG and IgM production in lymphocyte cultures prepared from the Peyer's patch (PP) and spleen. When purified B cells were cultured in the presence of vomitoxin, inhibition of IgA, IgG and IgM production was similarly observed. However, on 24-hr pulsed co-exposure to vomitoxin and the mitogen concanavalin A (ConA), CD4+/CD8+ cells were capable of inducing a three- to five-fold increase in production of IgA, but not IgG and IgM by cocultured B cells when compared with B cells cocultured with control T cells exposed to the mitogen only. When pulsed for 48 hr with ConA and toxin, CD4+ cells were similarly capable of causing a significant increase in IgA production by B cells. 48-hr pulsed exposure of CD4+ cells to ConA and vomitoxin resulted in significantly increased production of the T helper cytokines IL-4, IL-5 and IL-6 after 5 additional days of culture, compared with ConA-stimulated CD4+ cells alone. These results suggest that vomitoxin was capable of enhancing CD4+-mediated help for IgA production by B cells and that this could possibly be mediated by way of increased cytokine production.

L26 ANSWER 13 OF 37 MEDLINE DUPLICATE 7
94266212 Document Number: 94266212. PubMed ID: 8206429. Polyspecific and autoreactive IgA secreted by hybridomas derived from Peyer's patches of vomitoxin-fed mice: characterization and possible pathogenic role in IgA nephropathy. Rasooly L; Abouzied M M; **Brooks K H**; Pestka J J. (Department of Microbiology and Public Health, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1994 Apr) 32 (4) 337-48. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant **antibodies** were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenol that were representative of self and non-self antigens, approximately 95- of the monoclonal IgAs bound to at least one of the panel antigens and 80- bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition

in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 14 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
94:364738 The Genuine Article (R) Number: NQ428. POLYSPECIFIC AND AUTOREACTIVE IGA SECRETED BY HYBRIDOMAS DERIVED FROM PEYERS-PATCHES OF VOMITOXIN-FED MICE - CHARACTERIZATION AND POSSIBLE PATHOGENIC ROLE IN IGA NEPHROPATHY. RASOOLY L; ABOUZIED M M; **BROOKS K H**; PESTKA J J (Reprint). MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, 234 GM TROUT BLDG, E LANSING, MI, 48824 (Reprint); MICHIGAN STATE UNIV, DEPT FOOD SCI & HUMAN NUTR, E LANSING, MI, 48824; MICHIGAN STATE UNIV, DEPT MICROBIOL & PUBL HLTH, E LANSING, MI, 48824. FOOD AND CHEMICAL TOXICOLOGY (APR 1994) Vol. 32, No. 4, pp. 337. ISSN: 0278-6915. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A total of 122 immunoglobulin (Ig)A-producing hybridoma clones were isolated from the Peyer's patches of vomitoxin-fed BALB/c mice and the resultant **antibodies** were characterized for their antigenic specificity and pathogenic potential. When reactivity was tested against a panel consisting of DNA, sphingomyelin, thyroglobulin, collagen, casein, cardiolipin and bovine serum albumin conjugates of phosphorylcholine, inulin and trinitrophenol that were representative of self and non-self antigens, approximately 95- of the monoclonal IgAs bound to at least one of the panel antigens and 80- bound to more than one antigen. The polyspecificity of some of the monoclonal IgAs was further suggested by demonstrating the capacity of one antigen to inhibit binding of monoclonal IgA to another antigen. Protein staining and Western blotting of gradient native polyacrylamide gels, indicated that trimeric IgA predominated in the isolated monoclonal IgAs. Repeated injections of mice with representative monoclonal IgAs induced microhaematuria in three of four of the clones tested but not IgA deposition in the kidney glomerulus. In addition, three of the four monoclonal IgAs caused IgG and C3 deposition in the kidney mesangium. These and previous results suggest that dietary vomitoxin promotes the polyclonal activation and expansion of IgA-secreting B cells at the Peyer's patch level and that resultant polyspecific, autoreactive IgA may contribute to kidney pathogenesis.

L26 ANSWER 15 OF 37 MEDLINE DUPLICATE 8
95048595 Document Number: 95048595. PubMed ID: 7525472. B-1 cells in systemic autoimmune responses: IgM+, Fc epsilon Rdull B cells are lost during chronic graft-versus-host disease but not in murine AIDS or collagen-induced arthritis. Iciek L A; Waldschmidt T J; Griffiths M M; **Brooks K H.** (Department of Microbiology, Michigan State University, East Lansing 48824.) IMMUNOLOGICAL INVESTIGATIONS, (1994 Aug) 23 (4-5) 293-311. Journal code: 8504629. ISSN: 0882-0139. Pub. country: United States. Language: English.
AB The potential role of B-1 cells (i.e. the CD5+ B cell and "sister" B cell subsets) in autoimmunity is controversial. CD5+ B cells have been shown to secrete **antibodies** of similar specificity as those found in many systemic autoimmune diseases; in addition, increases in CD5+ B cell frequency have been reported in patients suffering from rheumatoid arthritis, Sjogren's syndrome, myasthenia gravis, insulin-dependent diabetes mellitus and Hashimoto's thyroiditis. Whether these increases are due to expansion of B-1 lineage cells in the human or due to activation-induced expression of CD5 by conventional B cells is unclear. In the present study, we used three murine models of systemic autoimmunity: murine acquired immunodeficiency syndrome (MAIDS), chronic graft-versus-host disease (cGvHD), and collagen-induced arthritis (CIA) to determine whether increases in B-1 cell frequency are universally seen in models of autoimmunity which are mechanistically distinct. In contrast to the aforementioned human systemic autoimmune diseases which exhibit an

increase in CD5+ B cell frequency, the percentage of CD5+ B cells declined in all three murine models of systemic autoimmune disease. Even though there was a decrease in the frequency of CD5+ B cells there was no change in the actual number of CD5+ B cells. Thus, the apparent decline in CD5+ B cell frequency was due to increases in either T cells, conventional Fc epsilon R+ B cells, or both. The only actual decline in a B cell subset was the loss of IgM+, Fc epsilon Rdull cells in both the spleen and peritoneal cavity of mice undergoing a chronic graft-versus-host reaction. Therefore, our data suggests that expansion of the B-1 subset does not occur as a general feature of murine systemic autoimmune disease. These observations, consistent with previous studies of Ig gene usage in autoreactive **antibodies**, support the view that expansion and differentiation of the CD5+ B cell subset is not a central event leading to autoantibody production.

L26 ANSWER 16 OF 37 MEDLINE DUPLICATE 9
94045239 Document Number: 94045239. PubMed ID: 8228625. Cytotoxic cell proteinase gene expression and cytolytic activity by anti-CD3-activated cytotoxic T lymphocytes is sensitive to cyclosporin A but is not dependent on interleukin-2 synthesis. Kaiser M; **Brooks-Kaiser J**; Fitzpatrick L; Bleackley R C; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1993 Nov) 54 (5) 458-64. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB We have examined the role of interleukin (IL) 2 in the expression of cytotoxic cell proteinases (CCP) 1 and 2, as well as in the induction of major histocompatibility complex (MHC)-unrestricted cytotoxic activity in murine T cell cultures following stimulation with anti-CD3 monoclonal **antibody**. A dramatic reduction in CCP-1 and CCP-2 gene expression and near absence of cytolytic activity was shown to occur in these cultures when the expression of IL-2 was inhibited by 10(-6) M cyclosporin A (CsA). The inhibitory effect of CsA could not be eliminated by the addition to culture of recombinant IL-2 at concentrations typically present in anti-CD3-stimulated T cell culture supernatants. Furthermore, when endogenous IL-2 (45-60 U/ml) present in anti-CD3-stimulated T cell cultures was neutralized with anti-mouse IL-2 **antibody** there was no effect on CCP-1 and CCP-2 mRNA expression and only a slight decrease in cytolytic activity. The expression of CCP-1 and CCP-2 gene products and the induction of MHC-unrestricted cytotoxic activity in anti-CD3-stimulated T cell cultures therefore occur independently of IL-2 synthesis but are regulated by a CsA-sensitive mechanism.

L26 ANSWER 17 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
93:126212 The Genuine Article (R) Number: KP121. COMPARISON OF THE INDUCTION OF ENDOTOXIN TOLERANCE IN ENDOTOXEMIA AND PERITONITIS BY MONOPHOSPHORYL LIPID-A AND LIPOPOLYSACCHARIDE. ASTIZ M E (Reprint); SAHA D C; **BROOKS K**; CARPATI C M; RACKOW E C. ST VINCENTS HOSP & MED CTR, NEW YORK MED COLL, DEPT MED, 153 W 11TH ST, NEW YORK, NY, 10011 (Reprint). CIRCULATORY SHOCK (MAR 1993) Vol. 39, No. 3, pp. 194-198. ISSN: 0092-6213. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We compared the induction of endotoxin tolerance with Salmonella minnesota monophosphoryl lipid A (MPL), a nontoxic derivative of lipid A, and S. minnesota endotoxin (LPS) in lethal endotoxemia and peritonitis. Lethal endotoxemia was induced by injecting 750 mug/mouse LPS intravenously. Cecal ligation and perforation was used to induce peritonitis. Tumor necrosis factor (TNF) was measured by immunoassay at 2 hr after lethal endotoxin infusion and 24 hr after peritonitis. A dose of 0.1 mug/mouse of MPL or LPS significantly reduced endotoxin mortality from 100% to 50% and 27%, respectively ($P < 0.05$). The LD50 for a 0.1 mug dose of MPL was 750 mug of LPS and the LD50 for a 0.1 mug dose of LPS was 115 mug of endotoxin ($P < 0.05$). TNF levels decreased linearly when increasing doses of MPL and LPS were used to induce tolerance. At higher pretreatment

doses of LPS, survival benefits were attenuated despite the reduction in TNF levels. A 25 mug dose of LPS reduced mortality from peritonitis from 93% to 45% ($P < 0.05$). Although MPL reduced short-term mortality, overall mortality was not significantly reduced despite using large doses of MPL. TNF levels peaked at 24 hr and were significantly lower than those following lethal endotoxemia. The induction of endotoxin tolerance by LPS and MPL is dose dependent, and LPS is modestly more effective in inducing endotoxin tolerance than MPL. Both LPS and MPL are significantly less effective in protecting against lethality from peritonitis.

L26 ANSWER 18 OF 37 MEDLINE DUPLICATE 10
94096351 Document Number: 94096351. PubMed ID: 8271238. Inhibition of DNA synthesis and IL-2 bioactivity in MLR by splenic pregnancy-associated natural suppressor cells involves the production of a TGF-beta 1-like molecule and a second distinct inhibitory factor. **Brooks-Kaiser J C**; Hoskin D W. (Department of Microbiology and Immunology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1993 Sep) 25 (1) 31-49. Journal code: 8001906. ISSN: 0165-0378. Pub. country: Ireland. Language: English.

AB Natural suppressor cells exhibiting a double-negative, immature T cell phenotype have been identified in maternal spleen during syngeneic murine pregnancy. In the present study, splenic pregnancy-associated natural suppressor (SPANS) cells are shown to express alpha/beta T cell receptors. SPANS cell-mediated inhibition of DNA synthesis by spleen cells responding in mixed lymphocyte reactions (MLR) is associated with a reduction in interleukin (IL)-2 bioactivity beginning after 96 h of culture. Although culture supernatants from suppressed MLR exhibit diminished ability to support the growth of IL-2-dependent CTLL-2 cells, SPANS cells themselves are unable to inhibit IL-2-driven CTLL-2 proliferation, suggesting that SPANS cells down-regulate IL-2 synthesis in MLR. IL-2 utilization in MLR is also inhibited by SPANS cells, since the addition of exogenous IL-2 fails to relieve the inhibitory effect of SPANS cells on lymphoproliferative responses in MLR. Flow cytofluorometric analysis reveals that MLR performed in the presence of SPANS cells contain normal percentages of CD4 and IL-2 receptor-bearing spleen cells. Thus, SPANS cells do not inhibit cellular proliferation in MLR by selectively interfering with clonal expansion of IL-2-producing helper T cells or by down-regulating IL-2 receptor expression. We have determined that SPANS cells inhibit DNA synthesis in MLR via the production of a transforming growth factor (TGF)-beta 1-like suppressor factor, since cellular proliferation in MLR is restored to normal levels in the presence of anti-TGF-beta 1 neutralizing **antibody**. However, IL-2 bioactivity in these cultures remains low in comparison to control MLR, suggesting the presence of a second distinct suppressor factor. Although the identity of this second inhibitory molecule has yet to be determined, neutralizing **antibody** studies have ruled out IL-10.

L26 ANSWER 19 OF 37 MEDLINE DUPLICATE 11
92308750 Document Number: 92308750. PubMed ID: 1535357. Soybean agglutinin-positive natural suppressor cells in mouse bone marrow inhibit interleukin 2 production and utilization in mixed lymphocyte reactions. Hoskin D W; Bowser D A; **Brooks-Kaiser J C**. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia, Canada.) JOURNAL OF LEUKOCYTE BIOLOGY, (1992 Jun) 51 (6) 649-56. Journal code: 8405628. ISSN: 0741-5400. Pub. country: United States. Language: English.

AB Although natural suppressor (NS) cells resident in bone marrow (BM) have been the subject of intensive study, the exact nature and mode of action of these potentially important immunoregulatory cells are still uncertain. Here we show that NS cells with potent inhibitory effects on mixed lymphocyte reactions (MLRs) can be isolated from BM of normal adult mice by agglutination with the plant lectin soybean agglutinin (SBA). Complement-dependent lysis of SBA receptor-bearing BM cells with **antibodies** to asialoGM1, Mac-1, Thy-1.2, J11d.2, and 2C1

phenotypic markers reveals the presence of at least two distinct populations of BM NS cells. Most of the SBA-binding BM cells with NS capacity have the null phenotype and resemble hematopoietic stem cells, and some inhibitory SBA+ BM cells express the 2C1 marker found on pregnancy-associated splenic NS cells and the J11d.2 antigen characteristic of B cells and immature T cells. Results of positive selective experiments confirmed these findings. The mechanism of natural suppression was also studied. Evidence is presented that SBA+ BM cells exert NS activity in MLRs by interfering with the production and utilization of interleukin 2. Indomethacin does not relieve natural suppression associated with SBA+ BM cells, indicating that prostaglandin synthesis is not a requirement for inhibitory function. However, neutralizing **antibodies** to transforming growth factor beta (TGF-beta) partially reverse the suppression mediated by SBA+ BM cells, suggesting that some BM NS cells may act through the release of an immunosuppressive molecule related to TGF beta.

L26 ANSWER 20 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
92:542319 The Genuine Article (R) Number: JM219. CD5 EXPRESSION IS MODULATED AS THE B-CELL MOVES THROUGH THE CELL-CYCLE. **BROOKS K H (Reprint)** ; YOL Y S; PESTKA J J. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES (04 MAY 1992) Vol. 651, pp. 259-260. ISSN: 0077-8923. Pub. country: USA. Language: ENGLISH.

L26 ANSWER 21 OF 37 MEDLINE DUPLICATE 12
92299374 Document Number: 92299374. PubMed ID: 1535063. Reactivity of monoclonal **antibody** 1E5.B5 with a novel phenotypic marker expressed on a murine natural suppressor cell subset. Hoskin D W; **Brooks-Kaiser J C**; Kaiser M; Murgita R A. (Department of Microbiology, Dalhousie University, Halifax, Nova Scotia.) HYBRIDOMA, (1992 Apr) 11 (2) 203-15. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.
AB Natural suppressor (NS) cells are antigen-nonspecific, MHC-independent immunoregulatory cells that are typically found in murine bone marrow (BM), newborn (NB) mouse spleen, and in splenic tissue of adult mice during pregnancy and following cyclophosphamide (CY) treatment. There has been a pressing need for the development of NS cell-specific monoclonal **antibodies** (mAb) since NS cells are generally described as null cells which lack the usual phenotypic markers of mature T cells, B cells, and macrophages. Here we present evidence that mAb 1E5.B5, which was raised in rats against murine splenic pregnancy-associated NS (SPANS) cells, recognizes a unique antigenic marker expressed by some, but not all, murine NS cells. In the presence of complement, mAb 1E5.B5 effectively eliminates SPANS activity, and diminishes NS activity of CY-treated spleen cells in mixed lymphocyte reactions (MLR). However, cytotoxic pretreatment with mAb 1E5.B5 had minimal effects on NS activity of BM and NB spleen cells. We also show that pregnancy spleen cells and CY-spleen cells with moderate NS activity in MLR can be positively selected for by "panning" with mAb 1E5.B5. In contrast, only weakly inhibitory cells are isolated from BM and NB spleen by this procedure. Cellular ELISA and flow cytometry confirm that mAb 1E5.B5 has specificity for pregnancy spleen cells and CY-spleen cells, as well as for NB spleen and BM cell preparations. Western blot analysis reveals that mAb 1E5.B5 reacts with a novel 50 kDa NS cell-associated antigen which we have termed NS-1. The NS-1 antigen is not present on other null cells such as natural killer (NK) cells and natural cytotoxic (NC) cells since cytotoxic pretreatment of pregnancy spleen cells with mAb 1E5.B5 does not affect **antibody**-dependent cell-mediated cytotoxicity, NK or NC activity.

L26 ANSWER 22 OF 37 MEDLINE
91339197 Document Number: 91339197. PubMed ID: 1931408. IL-2 and IL-5 both induce mu S and J chain mRNA in a clonal B cell line, but differ in

their cell-cycle dependency for optimal signaling. Takayasu H; **Brooks K H.** (Genetics Program, Michigan State University, East Lansing 48824.) CELLULAR IMMUNOLOGY, (1991 Sep) 136 (2) 472-85. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

AB We have found that a neoplastic Lyl+ B cell clone (BCL1-3B3) can be stimulated to secrete IgM by a Th1-derived cytokine, IL-2, and/or by a Th2-derived cytokine, IL-5. At suboptimal concentrations these interleukins acted synergistically to enhance IgM secretion. Both IL-2 and IL-5 induced increases in microseconds and J chain mRNA levels. In the presence of both ILs, increases in microseconds and J chain mRNA were additive and paralleled increases in IgM secretion. Using cells synchronized at the G1/S border with excess thymidine or in early G1 using isoleucine-deficient media, IL-2 and IL-5 differed in their cell-cycle dependency for signal transmission. IL-5 appeared to act preferentially in late G1 of the cell cycle. In contrast, IL-2 stimulated S and G2 phase cells slightly more efficiently than cells in G1 of the cell cycle. Furthermore, a twofold increase in high-affinity IL-2R was observed as the cells entered S phase. The results suggest that although IL-2 and IL-5 can independently and additively induce differentiation of the Lyl+ BCL1-3B3 cells, they differ in their point of action during the cell cycle.

L26 ANSWER 23 OF 37 MEDLINE

91007479 Document Number: 91007479. PubMed ID: 2145206. Elevated membrane IgA+ and CD4+ (T helper) populations in murine Peyer's patch and splenic lymphocytes during dietary administration of the trichothecene vomitoxin (deoxynivalenol). Pestka J J; Dong W; Warner R L; Rasooly L; Bondy G S; **Brooks K H.** (Department of Food Science and Human Nutrition, Michigan State University, East Lansing 48824.) FOOD AND CHEMICAL TOXICOLOGY, (1990 Jun) 28 (6) 409-20. Journal code: 8207483. ISSN: 0278-6915. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Recent investigations indicate that dietary exposure to the trichothecene vomitoxin increases total and antigen-specific serum immunoglobulin A (IgA) and glomerular IgA accumulation in mice. In this study, the effects of 25 ppm dietary vomitoxin on the histological and lymphocytic profile of component immune organs in the mucosal lymphocyte migratory pathway were evaluated in the B6C3F1 mouse. Vomitoxin administration resulted in marked stimulation of the size and frequency of germinal centres in Peyer's patches, mesenteric lymph nodes and the spleen. A slight increase in the percentage of B cells in the Peyer's patch was observed, although vomitoxin treatment had no effect on the percentage of B cells in the spleen. The percentage of IgA+ cells in Peyer's patches and spleen were approximately twice that of controls at 4, 8 and 12 wk of vomitoxin exposure whereas the percentage of IgG+ cells decreased in these two organs. Exposure to vomitoxin increased the percentage of T cells in Peyer's patches and the spleen. The percentage of CD4+ cells (T helper subset) increased slightly in Peyer's patches and more markedly (30-50%) in the spleen following vomitoxin treatment. Contrastingly, there was only a slight increase in the percentage of CD8+ cells (T cytotoxic/suppressor subset) in the spleens of vomitoxin-treated mice in comparison with controls, and no effect in Peyer's patches. The relative effects of vomitoxin on these two T cells populations was also reflected in increased CD4+: CD8+ ratios in Peyer's patches and spleen. These results are consistent with the hypothesis that dietary vomitoxin modulates normal regulation of the IgA response at the Peyer's patch level and that this is manifested in an altered lymphocyte distribution pattern in both the mucosal and systemic compartment. Notably increased levels of IgA+ and CD4+ cells are indicative of IgA-producing progenitors and T helper subsets, respectively, that in tandem could favour IgA hyperproduction and elevated IgA in serum.

L26 ANSWER 24 OF 37 SCISEARCH COPYRIGHT 2002 ISI R

91:259714 The Genuine Article R Number: FG852. CHARACTERIZATION OF A NEOPLASTIC B-CELL CLONE THAT SECRETES IGM IN RESPONSE TO TH2-DERIVED

LYMPHOKINES. **BROOKS K H (Reprint)**; OAKLEY C S; TAKAYASU H. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY (1990) Vol. 4, No. 6, pp. 339-348. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recent advances of T cell cloning have allowed the classification of T helper cells in terms of the lymphokines they secrete. The functional significance of segregating lymphokine production to unique T cell subsets is still being evaluated, but undoubtedly plays a key role in the regulatory mechanisms of the immune system. Initial studies have indicated that the Th1 cells which secrete IL-2 and IFN-gamma may be primarily responsible for augmenting cell-mediated responses, whereas Th2 cells, which release IL-4, IL-5, and IL-6, provide help for humoral responses. However, it is also known that B cells can respond to both IL-2 and IFN-gamma. This raises the question of the homogeneity of B lymphocyte activation requirements. Are all B cells responsive to all of the lymphokines with the end-result of stimulation depending largely on the relative concentrations of the various lymphokines, or are there B cell subsets which only respond to Th1-derived lymphokines and others which respond to Th2-derived lymphokines? Such differential activation requirements might be present to allow these subsets to play unique roles in immunological responses. Since B cell cloning techniques have not yet been developed to obtain a homogenous B cell population for studies of activation requirements, regulation of lymphokine receptors, and regulation of gene expression, we must utilize lymphokine-responsive neoplastic B cells. The vast majority of spontaneous B cell lymphomas appear to belong to a minor B cell subset which expresses the Ly1 marker. This subset is clearly not representative of the majority of splenic B cells. In this report, we have characterized the lymphokine response pattern of Ly1- B cell clones derived from a spontaneous tumor occurring in an AKR mouse.

Neoplastic B cell clones were generated from the 225 lymphoma, which secrete significant levels of IgM upon stimulation with lymphokines produced by type 2 T helper (Th2) cells. The 225 clones expressed a high-density of mIgM, varying densities of mIgD, and were mIgG and Ly1 negative. Th2-derived lymphokines found in D10.G4.1 SN will induce differentiation, as indicated by release of IgM in the culture SN. The 225 cells did not respond to IL-2, IFN-gamma, IL-1, or any combination of these lymphokines. Optimal differentiation occurred only when IL-4, IL-5, and IL-6 were present. The order of differentiative activity of these lymphokines was IL-5 > IL-4 > IL-6. The lack of IL-2 responsiveness in the face of IL-2R-alpha (p55) chain expression was due to the lack of high-affinity IL-2 receptors. In contrast, the IL-2 responsive clone BCL1-3B3 expresses approximately 950 high affinity IL-2R per cell. Thus, the 225-11 clone should provide a useful model system for the evaluation of the regulation of immunoglobulin gene expression mediated by Th2-derived lymphokines.

L26 ANSWER 25 OF 37 SCISEARCH COPYRIGHT 2002 ISI (R)
91:258713 The Genuine Article (R) Number: FJ252. ADRENOCORTICOTROPIN (ACTH) FUNCTIONS AS A LATE-ACTING B-CELL GROWTH-FACTOR AND SYNERGIZES WITH INTERLEUKIN-5. **BROOKS K H (Reprint)**. MICHIGAN STATE UNIV, DEPT MICROBIOL, E LANSING, MI, 48824 (Reprint). JOURNAL OF MOLECULAR AND CELLULAR IMMUNOLOGY (1990) Vol. 4, No. 6, pp. 327-337. Pub. country: USA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In recent years there has been considerable discussion of possible cross-regulatory mechanisms involving the immune system and the neuroendocrine system. Certainly, evidence of hormonal communication between these two systems would provide at least a partial explanation for the many anecdotal observations of physical and mental stress affecting disease course. In previous studies of a neoplastic lymphokine-responsive B cell clone, BCL1-3B3, we noted that these cells produced a lymphokine

which could affect normal B cell growth and viability. Physical characterization of this lymphokine indicated that its molecular weight was identical to that of the neuroendocrine hormone adrenocorticotropin (ACTH). Since Blalock and colleagues had reported the production of ACTH by virally-infected B cells, we have investigated whether ACTH can functionally mimic the BCL1-3B3-derived lymphokine. The neuroendocrine hormone adrenocorticotropin (ACTH) can increase in vitro murine B lymphocyte proliferation when added at physiologically relevant concentrations between 10(-9) to 10(-11) M. ACTH does not mimic the action of any lymphokine known to be required for B cell proliferation such as IL-2, IL-4, or IL-5. ACTH requires the presence of one or more of these known B cell stimulatory factors for its action and the most marked increase in B cell proliferation were noted in assays for IL-5 activity where 10(-10) M ACTH increased thymidine incorporation up to five-fold. Using two-stage assays, we determined that ACTH acts during the latter stages of B cell activation (i.e., 3-4 days after initial stimulation with either the combination of IL-4, GAMIg-Sepharose, and IL-1 or the combination of DxS and IL-5). These data indicate a direct role for a stress-induced neuroendocrine hormone in modulating the course of a humoral immune response.

L26 ANSWER 26 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1987:262595 Document No.: BR33:4491. INTERLEUKIN-2 INDUCES IGM SECRETION IN LYL+ NEOPLASTIC B CELLS BCL-1. **BROOKS K H**; KRAMMER P H; UHR J W; VITETTA E S. DEP. MICROBIOL., UNIV. TEX. HEALTH SCI. CENTER, SOUTHWESTERN MED. SCH., DALLAS, TEX. 75235.. GOLDSTEIN, G., J.-F. BACH AND H. WIGZELL (ED.). UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY NEW SERIES, VOL. 41. IMMUNE REGULATION BY CHARACTERIZED POLYPEPTIDES; STEAMBOAT SPRINGS, COLORADO, USA, JANUARY 25-FEBRUARY 1, 1986. XXVI+786P. ALAN R. LISS, INC.: NEW YORK, NEW YORK, USA. ILLUS. (1987) 0 (0), 305-314. CODEN: USMBD6. ISSN: 0735-9543. ISBN: 0-8451-2640-7. Language: English.

L26 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2002 ACS
1987:174381 Document No. 106:174381 Interleukin-2 induces IgM secretion in Ly1+ neoplastic B cells (BCL1). **Brooks, Kathryn H.**; Krammer, Peter H.; Uhr, Jonathan W.; Vitetta, Ellen S. (Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA). UCLA Symp. Mol. Cell. Biol., New Ser., Volume Date 1986, 41(Immune Regul. Charact. Polypept.), 305-14 (English) 1987. CODEN: USMBD6. ISSN: 0735-9543.
AB Cells from 2 neoplastic B cell clones have been used to exam. the effect of interleukin-2 (IL-2) on B cell differentiation. Cells from both clones express high levels of secretory IgM but relatively little secretory IgD; however, they differ in their expression of the Ly1 marker. The cells from the Ly1+ BCL1-derived (BALB/c) clone secrete IgM in response to purified and recombinant IL-2. This response can be blocked with monoclonal anti-IL-2 **antibodies**. In contrast, cells from a Ly1- neoplastic B cell clone from AKR mice (AKR-225) do not differentiate in response to IL-2 or IL-2 plus recombinant interferon. The cells from both the BCL1 clone and the AKR-225 clone can differentiate in response to B cell stimulatory factor(s) present in supernatants (SNs) of the alloreactive T cell line, PK 7.1. This PK 7.1 SN lacks significant IL-2 activity but does contain the differentiation factor for IgM. The different activation requirements of these Ly1+ and Ly1- neoplastic B cells is intriguing in light of both the assocn. of normal Ly1+ B cells with autoimmune disease and the prodn. of a B cell growth factor by the Ly1+ BCL1 clone but not the AKR-225 clone.

L26 ANSWER 28 OF 37 MEDLINE DUPLICATE 13
87034946 Document Number: 87034946. PubMed ID: 2945963. Recombinant IL 2 but not recombinant interferon-gamma stimulates both proliferation and IgM secretion in a Ly-1+ clone of neoplastic murine B cells (BCL1).
Brooks K H; Vitetta E S. JOURNAL OF IMMUNOLOGY, 1986 Nov 15, 137

(10) 3205-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We have used a lymphokine-responsive clone (3B3) of B leukemia cells (BCL1) to examine the effects of several recombinant and purified lymphokines. Cells from BCL1-3B3 were induced to secrete IgM in the presence of recombinant interleukin 2 (rIL 2) (10 to 50 U/ml); a concomitant increase in proliferation was observed. Recombinant interferon-gamma (rIFN-gamma) was a potent inhibitor of proliferation. In addition, rIFN-gamma did not induce an increase in IgM secretion and, when added to rIL 2-stimulated BCL1-3B3 cells, completely blocked IgM secretion at a concentration of 10 U/ml. Purified and recombinant IL 1 (rIL 1) had no significant effect on differentiation either alone or in combination with rIL 2 and/or rIFN-gamma. However, rIL 1 was able to synergize with rIL 2 in enhancing the proliferation of BCL1-3B3. The ability of cells to respond to rIL 2 was limited to the in vitro (Ly-1+) clones of BCL1 cells since the in vivo derived (Ly-1-) BCL1 cells did not differentiate in response to IL 2. Consistent with their functional response to rIL 2, cells from the in vitro clone (3B3) are IL 2-receptor-positive (IL-2R+) and the in vivo derived BCL1 cells are IL-2R-. A second set of neoplastic B cell clones derived from the AKR 225 lymphoma did not respond to rIL 2 even though they expressed receptors for IL 2 and could be induced by T cell supernatant to secrete IgM, thus indicating that expression of IL 2R is not the sole requirement for IL 2 responsiveness. The monoclonal anti-IL 2R **antibody** (7D4) mimicked IL 2 in its ability to stimulate differentiation of BCL1-3B3 cells. These data suggest that rIL 2 and the monoclonal anti-IL-2R **antibody** are capable of inducing a differentiative response in the Ly-1+ BCL1-3B3 cells that is functionally equivalent to the response evoked by the previously described lymphokine B cell differentiation factor for IgM (BCDF mu). Thus, two distinct lymphokines appear to be providing a similar signal to a clonal neoplastic B cell population. Furthermore, rIL 2 is capable of providing both a proliferative and a differentiative signal.

L26 ANSWER 29 OF 37 MEDLINE

85081355 Document Number: 85081355. PubMed ID: 3871214. Cell cycle-related expression of the receptor for a B cell differentiation factor. **Brooks K H**; Uhr J W; Vitetta E S. JOURNAL OF IMMUNOLOGY, (1985 Feb) 134 (2) 742-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Cloned, neoplastic B cells (BCL1) have been used to evaluate the expression of the receptor for the B cell differentiation factor, BCDF mu. These cells do not secrete IgM before stimulation with BCDF mu-containing T cell supernatants (SN). By inducing cell cycle synchrony in this homogeneous population, the expression of the BCDF mu receptor could be evaluated as a function of the cell cycle. Responsiveness to BCDF mu-containing SN is maximal when the cells are in S and G2 phases of the cell cycle, and a 2-hr exposure of cells to BCDF mu-containing SN during S/G2 results in optimal IgM secretion 5 days later. Cells in S/G2 are also maximally effective in absorbing BCDF mu activity from SN. These data support the hypothesis that B cells do not respond to differentiative signals until after they are committed to at least one round of cell division.

L26 ANSWER 30 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

84120729 EMBASE Document No.: 1984120729. T cell-derived lymphokines that induced IgM and IgG secretion in activated murine B cells. Vitetta E.S.; **Brooks K.**; Chen Y.-W.; et al.. Department of Microbiology, University of Texas Health Science Center, Dallas, TX 75235, United States. Immunological Reviews VOL. 78/- 137-157 1984. CODEN: IMREDZ. Pub. Country: Denmark. Language: English.

AB We have defined 2 lymphokine activities, termed BCDF.mu. and BCDF.gamma., which are present in the supernatants of T cell tumors, lines and hybridomas. These lymphokines appear to act directly on activated normal B

cells (or in the case of BCDF.mu., on BCL1 cells as well) to induce the synthesis and secretion of IgM or IgG1, respectively. These lymphokines are different from each other as well as from IL-1, IL-2, IFN.gamma., and conventional TRF. By molecular weight, BCDF.mu. is different from BCGF. The 2 BCDFs appear to bind to 2 different receptors on the cell surface and, thereby, to induce changes in the levels of isotype-specific mRNA and secreted immunoglobulin. The binding of BCDF.mu. to target cells appears to be cell-cycle related (optimal in G2S) and independent of T cells and macrophages. This has not been proven for BCDF.gamma.. It is possible that a subset of cells present in normal B cell populations, but not represented by the cloned BCL1 cells, is needed for BCDF.gamma. activity. Studies from other laboratories describing BCDF.gamma. (Severinson et al. 1982) BCDF.alpha. (Mayer et al. 1982, Kawanishi et al. 1983), and BCDF.epsilon. (Kishimoto & Ishizaka 1973, Hirashima et al. 1981) activities in T cell supernatants suggest that T cell-derived lymphokines may regulate the expression and/or secretion of several classes of immunoglobulin in activated B cells.

L26 ANSWER 31 OF 37 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1984:44777 Document No.: BR26:44777. LYMPHOKINE INDUCED DIFFERENTIATION OF CLONAL NEOPLASTIC B CELLS. **BROOKS K**; YUAN D; UHR J; KRAMMER P; VITETTA E S. UNIV. TEX. HEALTH SCI. CENT. DALLAS, DALLAS, TEX. 75235.. 67TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, CHICAGO, ILL., USA, APRIL 10-15, 1983. FED PROC. (1983) 42 (5), ABSTRACT 6101. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L26 ANSWER 32 OF 37 MEDLINE DUPLICATE 14
83192467 Document Number: 83192467. PubMed ID: 6601774.
Lymphokine-induced IgM secretion by clones of neoplastic B cells.
Brooks K; Yuan D; Uhr J W; Krammer P H; Vitetta E S. NATURE, (1983 Apr 28) 302 (5911) 825-6. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The induction of **antibody** secretion by B cells requires T-cell-derived factors1-5. Such factors have been described1,2,6-12 but the precise relationship among these various factors is not clear, and it has been difficult to demonstrate that these factors act directly on the B cell and do not exert their effect via T cells or macrophages. In this report we describe the direct induction of IgM synthesis and secretion in cloned lines of long-term tissue culture adapted neoplastic B cells (BCL1) by T-cell supernatants from phorbol-12-myristate 13-acetate (PMA)-induced EL-4 cells or concanavalin A (Con A)-induced 7.1.1a cells5,9. We have termed this activity BCDFmu (B-cell differentiation factor for IgM). The supernatants containing BCDFmu induce activated and neoplastic B cells to secrete IgM5 and the factor responsible is distinct from BCGF13, interleukin-2 (IL-2)5, the classical T-cell replacing factor (TRF) described by Schimpl and Wecker5, and immune interferon (IFN gamma)5.

L26 ANSWER 33 OF 37 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15
83152564 EMBASE Document No.: 1983152564. The correlation between the activation state of B cells and their capacity for in vitro propagation of immunologic memory. **Brooks K.H.**; Feldbush T.L.. Dep. Microbiol., Univ. Iowa, Iowa City, IA 52242, United States. Cellular Immunology 76/2 (213-223) 1983.
CODEN: CLIMB8. Pub. Country: United States. Language: English.
AB The B-cell population responsible for in vitro antigen-mediated proliferation and expansion of the memory B-cell population is a large activated blast. Such cells predominate early after antigen priming and can be regenerated by adjuvant (Bordetella pertussis) stimulation in vivo. Although these cells are proliferating in vivo, additional stimuli are needed for expansion of the memory population in vitro. These triggering requirements include specific antigen (DNP-OVA) and the assistance of adherent accessory cells. Although T cells are present in the culture,

their role in the propagation of memory is not completely clear. Using the unrelated antigen, sheep erythrocytes, we have shown that 'bystander' T-cell help can mediate differentiation of these memory B-cell blasts to AFC, but it cannot induce expansion of the memory-cell population. However, the fact that the TI-2 antigen DNP-Ficoll is a relatively ineffective inducer of memory-cell propagation (inducing an expanded response which is less than 10% of that induced by the T-cell-dependent antigen, DNP-OVA) suggests that T cells may be involved, possibly via production of B-cell growth factor. Thus, the minimal requirements for triggering the propagation of B-cell memory include (i) a blastogenic signal which can be mediated by adjuvant, (ii) specific antigen, and (iii) adherent accessory-cell help.

L26 ANSWER 34 OF 37 MEDLINE DUPLICATE 16
81265503 Document Number: 81265503. PubMed ID: 7021678. Generation of **antibody**-mediated regulation during in vitro clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 963-7. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

L26 ANSWER 35 OF 37 MEDLINE
81265502 Document Number: 81265502. PubMed ID: 7021677. In vitro antigen-mediated clonal expansion of memory B lymphocytes. **Brooks K H**; Feldbush T L. JOURNAL OF IMMUNOLOGY, (1981 Sep) 127 (3) 959-63. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB An in vitro model for the propagation and expansion of the memory B lymphocyte population is described. DNP-BGG immune cells were mixed with OVA immune cells and challenged immediately with DNP-OVA. After the 1st response had begun to wane, the cells were rechallenged with DNP-OVA (day 11 of culture). An average of 13-fold more PFC were observed after delayed challenge (day 11). This expansion in the PFC response was an antigen-dependent process and did not involve recruitment of new memory cells from the virgin lymphocyte pool. The level of expansion of the memory cell pool was also calculated using limiting dilution analysis and was found to fall in a range of 16- to 67-fold increase in precursor frequency. In addition to the expansion of the memory B cell population, we also observed the development of 2 immunoregulatory cycles previously observed only in vivo. First, in the presence of persistent antigen, a cyclical PFC response was seen. Second, after day 10 of culture, optimal PFC numbers were observed only when DNP-lysine was added to the plaque assay. Such hapten-augmentable PFC responses have been reported by other investigators as indicative of anti-idiotypic regulation. This possibility is examined more extensively in the following communication.

L26 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2002 ACS
1982:558292 Document No. 97:158292 Isolation and characterization of an .alpha.1-antitrypsin-related glycoprotein from human liver. Glew, Robert H.; Zidian, J. L.; Chiao, J. P.; Kuhlenschmidt, T.; Iammarino, Richard M.; **Brooks, K. P.** (Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA). Electrophor. '81 [Eighty-One], Proc. Int. Conf., 3rd, 511-21. Editor(s): Allen, Robert Chadbourne; Arnaud, Philippe. de Gruyter: Berlin, Fed. Rep. Ger. (English) 1981. CODEN: 48KUAG.
AB A 68,000-dalton glycoprotein which cross-reacts with **antibody** to human plasma .alpha.1-antitrypsin (I) was purified from the 100,000-g supernatant of human liver. This glycoprotein (I-CRM) had 9.5% of the immunoreactivity of I and no antiproteinase activity. Isoelec. focusing resolved I-CRM into 2 fractions which differed in immunoreactivity. Carbohydrate and amino acid analyses were carried out. I-CRM, which differed from I in mol. wt., also differed substantially in CNBr- and chymotrypsin-derived fragments. The basis of the relatedness of plasma I and I-CRM, which represents only approx.0.1% of liver protein content, is not known; however, as immunospecificity was the major criteria for

purifn. the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

L26 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
80132519 Document Number: 80132519. PubMed ID: 6153580. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool: effect of time and antigen. **Brooks K H**; Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, (1980 Mar 15) 50 (2) 392-404. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

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1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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CA SUBSCRIBER PRICE	-0.62	-0.62

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L3 3 DUP REMOVE L2 (8 DUPLICATES REMOVED)

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L3 ANSWER 1 OF 3 MEDLINE
2002224456 Document Number: 21957817. PubMed ID: 11962725. DUPLICATE 1
Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S ; Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody** , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L3 ANSWER 2 OF 3 MEDLINE
2000150073 Document Number: 20150073. PubMed ID: 10684997. DUPLICATE 2
In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T; Kloetzer W S;** Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E.** (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

purifn. the report of frequent findings of I-CRM in normal and diseased liver may be accounted for by the present observation.

L26 ANSWER 37 OF 37 MEDLINE DUPLICATE 17
80132519 Document Number: 80132519. PubMed ID: 6153580. The generation of memory B-cell subpopulations capable of proliferation and expansion of the pool: effect of time and antigen. **Brooks K H;** Feldbush T L; van der Hoven A. CELLULAR IMMUNOLOGY, (1980 Mar 15) 50 (2) 392-404. Journal code: 1246405. ISSN: 0008-8749. Pub. country: United States. Language: English.

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	CHEMLIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 1 Mar 02
NEWS 6	Mar 19	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TROTHERMO no longer available
NEWS 9	Mar 29	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 29	LIPINSKI CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.

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NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14  Apr 09  ZDB will be removed from STN
NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available
NEWS 19  Jun 03  New e-mail delivery for search results now available
NEWS 20  Jun 10  MEDLINE Reload
NEWS 21  Jun 10  PCTFULL has been reloaded
NEWS 22  Jul 02  FOREGE no longer contains STANDARDS file segment

NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:41:45 ON 05 JUL 2002

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 14:41:57 ON 05 JUL 2002

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=> s reff m?/au or kloetzer w?/au or nakamura t?/au
L1        42543 REFF M?/AU OR KLOETZER W?/AU OR NAKAMURA T?/AU

=> s l1 and cd23 antibody
L2           11 L1 AND CD23 ANTIBODY
```

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3 3 DUP REMOVE L2 (8 DUPLICATES REMOVED)

=> d l3 1-3 cbib abs

L3 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002224456 Document Number: 21957917. PubMed ID: 11962725. Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells. Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S ; Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody** , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs). RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L3 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T; Kloetzer W S;** Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E.** (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED(R)) monoclonal antibodies. PRIMATIZED(R) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED (R) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23 antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23 antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS

1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors (Molly) and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, N1+Neomycin phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23** **antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.21	15.42
DISCOUNT AMOUNTS FOR QUALIFYING ACCOUNTS		
CA SUBSCRIBER PRICE	-1.62	-1.62

STN INTERNATIONAL LOGOFF AT 14:43:19 ON 15 JUL 2002

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LOGINID:SSSPTA1644PNH

PASSWORD:
TERMINAL ENTER 1, 2, 3, OR ? :2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded
NEWS 22	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 23	Jul 19	NTIS to be reloaded July 28, 2002
NEWS 24	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 08:24:54 ON 24 JUL 2002

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 08:25:09 ON 24 JUL 2002

FILE 'EMBASE' ENTERED AT 08:25:09 ON 24 JUL 2002

FILE 'BIOSIS' ENTERED AT 08:25:09 ON 24 JUL 2002

FILE 'SCISEARCH' ENTERED AT 08:25:09 ON 24 JUL 2002

FILE 'CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002

=> s chimeric CD23
L1 15 CHIMERIC CD23

=> s l1 and antibod?
L2 6 L1 AND ANTIBOD?

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)

=> d l3 1-2 cbib abs

L3 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by **antibodies** or soluble CD23 induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonic@unice.it) . BLOOD, (2000 Jun 15) 95 (12) 3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger RNA (mRNA) expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of

CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3868-3877)

L3 ANSWER 2 OF 2 SCISEARCH COPYRIGHT 2002 ISI (R)
1998:947017 The Genuine Article (R) Number: 146NG. Production of a chimeric form of CD23 that is oligomeric and blocks IgE binding to the Fc epsilon RI. Kelly A E; Chen B H; Woodward E C; Conrad D H (Reprint). VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, BOX 980678, MCV STN, RICHMOND, VA 23298 (Reprint); VIRGINIA COMMONWEALTH UNIV, DEPT MICROBIOL & IMMUNOL, RICHMOND, VA 23298. JOURNAL OF IMMUNOLOGY (15 DEC 1998) Vol. 161, No. 12, pp. 6696-6704. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767. Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The low affinity receptor for IgE (Fc epsilon RII/CD23) has previously been shown to interact with IgE with a dual affinity. Three chimeric constructs were created containing the lectin domain (amino acids 172-188) or the ''neck'' and lectin domain (amino acids 157-188) attached to subunits of oligomeric proteins. All chimeras were incapable of interacting with IgE with either a high or low affinity, indicating that the alpha-helical stalk of CD23 is important for orienting the lectin heads such that an interaction with IgE can occur. This concept received further support in that a **chimeric CD23** composed of the human CD23 stalk and the mouse CD23 lectin head bound mouse IgE with a dual affinity, but could only bind rat IgE with a low affinity. Effort was next concentrated on a construct consisting of the entire extracellular (EC)region of CD23, A mutation to the first cleavage site of CD23 (C1M) resulted in a more stable molecule as determined by a decrease of soluble CD23 release, A soluble chimeric EC-C1M was prepared by attaching an isoleucine zipper to the amino terminus (1zEC-C1M), The interaction with IgE by 1zEC-C1M was found to be superior to that seen with EC-CD23. The IzEC-C1M could inhibit binding of IgE to both CD23 and the high affinity receptor for IgE, Fc epsilon RI, providing further evidence for a strong interaction with IgE, Fc epsilon RT inhibition (similar to 70-) was seen at equimolar concentrations of IzEC-C1M, implying the effectiveness of this chimera and suggesting its potential therapeutic value.

=> s humanized anti CD23
L4 1 HUMANIZED ANTI CD23

=> d l4 cbib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
2000:457197 Document No. 133:57697 Enhanced proteins production in cell culture stimulated by unusually low alkanoic acid concentrations. Islam, Seema; Sharp, Nigel Alan (Glaxo Group Limited, UK). PCT Int. Appl. WO 2000039282 A1 20000706, 21 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English . CODEN: PIXXD2. APPLICATION: WO 1999-EP10157 19991221. PRIORITY: GB 1998-28684 19981223.
AB A process is provided for the prodn. of a protein by culturing eukaryotic cells that constitutively secrete the protein into a medium contg. an alkanoic acid or its salt at a maintained concn. of less than 1.1mM. Thus, NSO cells transfected with an IgG1 **humanized anti -CD23** antibody was cultured for 56 days in a draw and fill

repeated batch mode in a medium contg. 0 to 0.10 mM sodium butyrate. Results showed that cells cultured in the presence of 0.075mM butyrate showed a marked increase in antibody prodn. over the control.

=> s monoclonal
L5 727044 MONOCLONAL

=> s l5 and human CD23
4 FILES SEARCHED...
L6 43 L5 AND HUMAN CD23

=> s l6 and chimeric
L7 7 L6 AND CHIMERIC

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8 3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946 Document No.: PREV200200370946. Antibodies against the stalk region of huCD23 block binding of IgE and inhibit in vitro IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil, Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad, Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language: English.
AB The stalk region of **human CD23** comprising a.a. 48-153 was expressed in E. coli and purified. In addition a **chimeric human CD23** was prepared consisting of the extracellular region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal antisera were produced in rabbits and shown to block binding of IgE to CD23 both on cell surfaces as well as the interaction of LZ-CD23 with IgE in an ELISA based assay. The antisera was also shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated human PBL model. The inhibition was dose dependent and essentially complete blockage of IgE production was seen at a relatively low dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells indicated little if any endocytosis and/or protection from cleavage induced by the anti-stalk. **Monoclonal** antibodies against the human stalk have also been prepared and these are being analyzed for the capacity to inhibit IgE binding and IgE synthesis, as well as compare their efficacy to the anti-lectin mabs. The results indicate that targeting the stalk region is efficacious with respect to blocking IgE production.

L8 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:186695 Document No.: PREV200200186695. Induction of apoptosis by IDEC-152 (anti-CD23) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.
AB IDEC-152 is a primatized **monoclonal** antibody to **human CD23**, the low-affinity receptor for IgE on B cells that has been implicated in the regulation of IgE synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses IgE synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also

expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a **chimeric monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L8 ANSWER 3 OF 3 MEDLINE DUPLICATE 1

2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII), is involved in regulation of IgE synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct **chimeric** macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-CD23 antibodies inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

=> d his

FILE 'HOME' ENTERED AT 09:24:54 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002

L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBOD?
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23
L7 7 S L6 AND CHIMERIC
L8 3 DUP REMOVE L7 (4 DUPLICATES REMOVED)

=> s l5 and chimeric CD23
L9 1 L5 AND CHIMERIC CD23

=> d l9 cbib abs

L9 ANSWER 1 OF 1 MEDLINE
2000384038 Document Number: 20304490. PubMed ID: 10845922. Engagement of CD11b and CD11c beta2 integrin by antibodies or soluble CD23 induces IL-1beta production on primary human monocytes through mitogen-activated protein kinase-dependent pathways. Rezzonico R; Chicheportiche R; Imbert V; Dayer J M. (Division of Immunology and Allergy, Clinical Immunology Unit (Hans Wilsdorf Laboratory), Department of Internal Medicine, University Hospital, Geneva, Switzerland.. rezzonic@unice.it) . BLOOD, (2000 Jun 15) 95 (12) 3868-77. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB beta2 integrins are involved in the recruitment of leukocytes to inflammatory sites and in cellular activation. We demonstrate that ligation of CD11b (Mac-1, CR3) or CD11c (p150, CR4) alpha chains of beta2 integrins by mAbs or soluble **chimeric CD23** (sCD23) on human freshly isolated monocytes rapidly stimulates high levels of interleukin-1beta production. This induction takes place at the transcriptional level and is regulated by members of the mitogen-activated protein kinase (MAPK) family. Indeed, stimulation of monocytes through engagement of CD11b or CD11c results in the phosphorylation and activation of ERK1, ERK2, and p38/SAPK2 MAP kinases. U0126, a potent inhibitor of the upstream activator of ERK1/2, ie, MEK1/2, suppresses IL-1beta messenger RNA (mRNA) expression in a dose-dependent fashion, showing the implication of this pathway in the transcriptional control of IL-1beta production. On the other hand, inhibition of p38 by SB203580 indicates that this MAPK is involved in the control of IL-1beta production at both transcriptional and translational levels. Together these data demonstrate that ligation of CD11b and CD11c beta2 integrins by mAbs or sCD23 fusion proteins triggers the activation of 2 distinct MAPK signaling pathways that cooperate in controlling IL-1beta synthesis at different levels. (Blood. 2000;95:3868-3877)

=> s l5 and humanized CD23
L10 0 L5 AND HUMANIZED CD23

=> d his

FILE 'HOME' ENTERED AT 09:24:54 ON 24 JUL 2002

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 08:25:09 ON 24 JUL 2002
L1 15 S CHIMERIC CD23
L2 6 S L1 AND ANTIBOD?
L3 2 DUP REMOVE L2 (4 DUPLICATES REMOVED)
L4 1 S HUMANIZED ANTI CD23
L5 727044 S MONOCLONAL
L6 43 S L5 AND HUMAN CD23

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L7              7 S L6 AND CHIMERIC
L8              3 DUP REMOVE L7 (4 DUPLICATES REMOVED)
L9              1 S L5 AND CHIMERIC CD23
L10             0 S L5 AND HUMANIZED CD23

=> s l6 and IgE
L11            38 L6 AND IGE

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12            17 DUP REMOVE L11 (21 DUPLICATES REMOVED)

=> d l12 1-17 cbib abs

L12  ANSWER 1 OF 17  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:370946  Document No.: PREV200200370946. Antibodies against the stalk
     region of huCD23 block binding of IgE and inhibit in vitro
     IgE synthesis. Caven, Timothy Hays (1); Ma, Check (1); Beavil,
     Rebecca; Beavil, Andrew; Ghirlando, Rodolpho; Gould, Hannah; Conrad,
     Daniel (1). (1) Virginia Commonwealth University, 1217 East Marshall
     Street, Richmond, VA, 23298 USA. FASEB Journal, (March 22, 2002) Vol. 16,
     No. 5, pp. A1239. http://www.fasebj.org/. print. Meeting Info.: Annual
     Meeting of Professional Research Scientists on Experimental Biology New
     Orleans, Louisiana, USA April 20-24, 2002 ISSN: 0892-6638. Language:
     English.
AB   The stalk region of human CD23 comprising a.a. 48-153
     was expressed in E. coli and purified. In addition a chimeric
     human CD23 was prepared consisting of the extracellular
     region of CD23 linked to a modified leucine zipper (LZ-CD23). Polyclonal
     antisera were produced in rabbits and shown to block binding of
     IgE to CD23 both on cell surfaces as well as the interaction of
     LZ-CD23 with IgE in an ELISA based assay. The antisera was also
     shown to inhibit IgE synthesis in an anti-CD40/IL-4 stimulated
     human PBL model. The inhibition was dose dependent and essentially
     complete blockage of IgE production was seen at a relatively low
     dose of anti-stalk. FACS analysis using CD23+B lymphoblastoid cells
     indicated little if any endocytosis and/or protection from cleavage
     induced by the anti-stalk. Monoclonal antibodies against the
     human stalk have also been prepared and these are being analyzed for the
     capacity to inhibit IgE binding and IgE synthesis, as
     well as compare their efficacy to the anti-lectin mabs. The results
     indicate that targeting the stalk region is efficacious with respect to
     blocking IgE production.

L12  ANSWER 2 OF 17  CAPLUS  COPYRIGHT 2002 ACS
2001:747174  Document No. 135:287537  Inhibitors for the formation of soluble
     human CD23 and their use in treatment of diseases.
     Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp.
     DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL,
     SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW.
     APPLICATION: EP 2000-107515 20000407.
AB   A pharmaceutical compn. for the treatment or prophylaxis of disorders is
     described in which the overprodn. of sCD23 is implicated. This compn.
     comprises an inhibitor for the formation of human sol. CD23 which
     inhibitor decreases or blocks selectively the activity of the
     metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in
     human B-cell lines. Also described is a pharmaceutical compn. wherein the
     inhibitor for the formation of human sol. CD23 is a monoclonal
     or polyclonal antibody directed against the metalloprotease ADAM9 or
     wherein the inhibitor is an antisense oligonucleotide which is specific
     for c-myc. Such a pharmaceutical compn. may be used in a method for
     selectively inhibiting the formation of ADAM9 as well as the formation of
     sCD23. It is a suitable medicament against inflammatory disorders,
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autoimmune diseases and allergy.

L12 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2002:196695 Document No.: PREV200200186685. Induction of apoptosis by IDEC-152 (anti-CD23) in lymphoma cells. Pathan, Nuzhat (1); Hariharan, Kandasamy (1); Hopkins, Michael; Saven, Alan; Reff, Mitchell (1); Hanna, Nabil (1); Grint, Paul (1). (1) IDEC Pharmaceuticals, San Diego, CA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 367a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.

AB IDEC-152 is a primatized **monoclonal** antibody to **human CD23**, the low-affinity receptor for **IgE** on B cells that has been implicated in the regulation of **IgE** synthesis. In vitro and in vivo data have demonstrated that IDEC-152 suppresses **IgE** synthesis. IDEC-152 is currently in clinical trials for use in allergic asthma. CD23 is also expressed at high levels in certain B-cell malignancies, in particular Chronic Lymphocytic Leukemia (CLL). Multiple therapeutic agents for lymphomas including cytotoxic drugs as well as protein kinase modulators utilize apoptosis as the common pathway of inducing cell death. Rituxan, a chimeric **monoclonal** antibody to the B cell antigen CD20 that has been approved by the US Food and Drug Administration for the treatment of non-Hodgkins lymphoma (NHL), is also believed to work in part through the same mechanism. In the present study, we found that IDEC-152 could induce a dose-dependent apoptosis, assessed by FACS-based detection of activated caspase 3, in certain CD23 positive human lymphoma cell lines. Apoptosis was found to be dependent on IDEC-152 cross-linking with goat anti-human IgG F(ab)2 fragments. More than 60% of the cells showed activated caspase 3 with 10 ug/mL IDEC-152. Doses as low as 0.1 ug/mL resulted in apoptosis induction of apprx10%. Low doses of IDEC-152 were found to enhance Rituxan-induced apoptosis in SKW cells. In addition, IDEC-152 mediated a strong antibody dependent cellular cytotoxicity (ADCC) activity in vitro. Furthermore, in a disseminated human lymphoma/SCID murine model, it showed antitumor activity both as a monotherapy and in combination with Rituxan. Since CLL cells express high levels of CD23, IDEC-152 might be effective in inducing apoptosis in CLL cells. Studies addressing apoptosis induction in fresh CLL cells by IDEC-152 as a single agent as well as in combination with Rituxan or chemotherapy may support the rationale for the initiation of clinical trials in CLL patients.

L12 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320835. Gamma-1 anti-**human CD23 monoclonal** antibodies. Reff, Mitchell E. (1); Kloetzer, William S.; Nakamura, Takehiko. (1) San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-**human CD23 monoclonal** antibodies containing human gamma 1 constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L12 ANSWER 5 OF 17 MEDLINE DUPLICATE 1
2001151173 Document Number: 21515173. PubMed ID: 11694997. In vitro **IgE** inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao W; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.

INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for **IgE** (FcvarepsilonRII), is involved in regulation of **IgE** synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of **IgE** complexes to CD23 positive cells and also inhibited the production of **IgE** in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited **IgE** production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in **IgE** inhibition. An F(ab')(2) of p5E8G1 did not inhibit **IgE** production but did interfere with **IgE** inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits **IgE** production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit **IgE** production. These data imply that the mechanism by which anti-CD23 antibodies inhibit **IgE** production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit **IgE** production.

L12 ANSWER 6 OF 17 MEDLINE

2000150237 Document Number: 20150237. PubMed ID: 10684962.

Characterization of novel FcepsilonRII/CD23 isoforms lacking the transmembrane (TM) segment in human cell lines. Yoshikawa T; Matsui M; Gon Y; Yoshioka T; Hirama M; Lynch R G; Naito K; Yodoi J. (Institute for Virus Research, Kyoto University, 53 Kawahara-cho, Sakyo-ku, Kyoto, Japan.) MOLECULAR IMMUNOLOGY, (1999 Dec) 36 (18) 1223-33. Journal code: 7905289. ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Human FcepsilonRII/CD23 is an approximately 45 kDa type II transmembrane glycoprotein belonging to the C-type animal-lectin family, and has two isoforms (a and b) that only differ in their intracytoplasmic tails. We previously found that in several human and mouse cell lines there were two additional CD23 transcripts (a' and b') lacking the exon 3 that encodes the entire transmembrane segment and a part of cytoplasmic tails. In this study, we analyzed the putative CD23a' and CD23b' products at protein levels and characterized with rabbit polyclonal antibodies against novel amino-acid sequences of the putative CD23a' and CD23b' molecules (anti-CD23a' Ab, anti-CD23b' Ab). Western blots in COS cells transfected with CD23a' or CD23b' cDNA as well as in vitro translation assays showed that the a' and b' CD23 transcripts were translated to about 40 kDa molecules. These 40 kDa molecules were also recognized by a polyclonal antibody against 25 kDa soluble fragment of **human CD23**. We also found that human cells having mRNAs for CD23a' and CD23b' expressed protein products recognized specifically by anti-CD23a' or anti-CD23b' Ab, respectively. In addition, the CD23a' and CD23b' molecules in transfected COS cells were resistant to Endo H f and PNGase F, although these truncated forms as well as the membrane-associated forms had an asparagine residue responsible for the N-linked glycosylation. Taken together, our results show that the a' and b' CD23 transcripts are expressed and translated in human lymphoid cells and that their translated products are retained in the cytoplasm where they might play an unique regulatory role in the expression of the full-length CD23 on the cell surface.

L12 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2

1999:275763 Document No.: PREV199900275763. In vitro suppression of **IgE** synthesis by a primatized **monoclonal** antibody (mab) against **human CD23** antigen. Li, Yan-Ping; Kloetzer, William; Nakamura, Takehiko (1); Chen, Agnes; Brams, Peter; Hariharan, Kandasamy; Chamat, Soulaima; Cao, Xianjun; LaBarre, Michael; Chinn, Paul; Morena, Ron; Shestowsky, William; Hanna, Nabil; Reff, Mitchell. (1) Seikagaku Corp., Tokyo Japan. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A989. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April 17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L12 ANSWER 8 OF 17 MEDLINE DUPLICATE 3

1999111232 Document Number: 99111232. PubMed ID: 9893160. Upregulated surface expression of intracellularly sequestered Igepsilon receptors (FcepsilonRII/CD23) following activation in human peripheral blood eosinophils. Sano H; Munoz N M; Sano A; Zhu X; Herrnreiter A; Choi J; Leff A R. (Department of Medicine, Section of Pulmonary and Critical Care Medicine.) PROCEEDINGS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, (1999 Jan-Feb) 111 (1) 82-91. Journal code: 9514310. ISSN: 1081-650X. Pub. country: United States. Language: English.

AB We investigated the regulation, secretion, and surface expression of the low-affinity FcepsilonRII receptor (CD23) in eosinophils isolated from human blood using multiple **monoclonal** antibodies (mAbs) directed at different epitopes of **human CD23**. Substantial surface expression of CD23 was not demonstrated in the resting state. Mean fluorescence intensity (MFI) measured by flow cytometry was 7. 1 +/- 0.8 for 9P25 mAb (p = NS) and 15.7 +/- 3.8 for BU38 mAb (p <. 04) versus 5.3 +/- 1.0 for IgG1 isotype control Ab. By contrast, MFI using BU38 mAb was 154 +/- 18 for JY-B lymphocytes (p <.0001 versus eosinophils). Despite weak surface expression, eosinophil permeabilization demonstrated substantial intracellular expression of CD23; MFI was 33.6 +/- 5.2 for 9P25 mAb versus 4.4 +/- 0.43 for IgG control (p <.001). Western blot analysis using both positive and negative controls demonstrated immunological identity with CD23 on JY-B lymphocytes. Activation of eosinophils caused rapid translocation of CD23 to the surface membrane (160 +/- 33 MFI; p <. 005), which was maximal within 30 sec. Secretory CD23 was detected within the perfusate also at 30 sec and was fully reinternalized at 10 min. This is the first demonstration of the presence of intracellular CD23 in human eosinophils. Our data indicate that eosinophils rarely express CD23 on their surface but are capable of transient high-level expression and secretion with rapid reuptake of intracellular stores of CD23.

L12 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS

1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human CD23 monoclonal** antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp.). PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. English . CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980213. PRIORITY: US 1997-803095 19970221.

AB **Monoclonal** antibodies which specifically bind **human CD23**, the low affinity receptor for **IgE** FceRII/CD23 , and contain either a human gamma-1 or human gamma-3 const. domain, are

disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

L12 ANSWER 10 OF 17 MEDLINE DUPLICATE 4
97351082 Document Number: 97351082. PubMed ID: 9207458. Inhibition of apoptosis in a human pre-B-cell line by CD23 is mediated via a novel receptor. White L J; Ozanne B W; Graber P; Aubry J P; Bonnefoy J Y; Cushley W. (Institute of Biomedical & Life Sciences, University of Glasgow, Scotland, UK.) BLOOD, (1997 Jul 1) 90 (1) 234-43. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB **Human CD23** is a 45-kD type II membrane glycoprotein, which functions as a low-affinity receptor for **IgE** and as a ligand for the CD21 and CD11b/CD11c differentiation antigens. CD23 is released from the surface of cells as soluble fragments, and a 25-kD species of soluble CD23 (sCD23) appears to act as a multifunctional cytokine. In this report, sCD23 is shown to sustain the growth of low cell density cultures of a human pre-B-acute lymphocytic leukemia cell line, SMS-SB: no other cytokine tested was able to induce this effect. Flow cytometric analysis indicates that sCD23 acts to prevent apoptosis of SMS-SB cells. SMS-SB cells cultured at low cell density possess low levels of bcl-2 protein. Addition of sCD23 to cells at low cell density maintained bcl-2 expression at levels equivalent to those observed in SMS-SB cells cultured at higher cell densities. No CD23 mRNA was found in SMS-SB cells, ruling out an autocrine function for CD23 in this cell line model. Although SMS-SB cells do not express the known receptors for CD23, namely CD21, CD11b-CD18, or CD11c-CD18, the cells specifically bind CD23-containing liposomes, but not glycophorin-containing liposomes. Binding of CD23-containing liposomes is inhibited by anti-CD23 but not by anti-CD21 or anti-CD11b/c **monoclonal** antibodies. The data show that sCD23 prevents apoptosis of the SMS-SB cell line by acting through a novel receptor.

L12 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1996:463188 Document No.: PREV199699185544. Mechanism of T cell subsets and cytokines in the regulation of **IgE** production in exogenous asthma. Wang Danqi, Xia Guoguang (1); Zhao Shulin; et al.. (1) Dep. Respiratory Med., Beijing Ji Shui Tan Hosp., Beijing 100035 China. Zhonghua Weishengwuxue He Mianyixue Zazhi, (1996) Vol. 16, No. 4, pp. 299-301. ISSN: 0254-5101. Language: Chinese. Summary Language: Chinese; English.

AB The peripheral blood of 30 cases of asthma and 30 control adults were measured for T cell subsets with indirect Immunofluorescence of **monoclonal** antibodies, for **IgE**, IL-4 with ELISA, for IL-2 with F12-cell line-biological method, for IL-6 with IL-6-dependent cell line 7TD1 intake method and for CD23 with anti **human CD23** McAb. The mechanism of T cells and cytokines in the regulation of **IgE** production in asthma and the effect of cytokines on the pathogenesis of asthma were also studied. The results showed that the levels of **IgE**, IL-4, IL-2, CD23, CD8+ as well as the ratio of CD4/CD8+ in cases of their acute stage were significantly different from those in their remission stage and normal controls (P lt 0.01). In their remission stage, there was no significant **IgE** difference between cases and control (P gt 0.05). And there were significant differences of CD8+ CD4/CD8 ratio between cases and normal controls (P lt 0.01). There was no significant difference of CD3, CD4, IL-6 among three groups (P gt 0.05). It indicated that the increased production of **IgE** antibody was the key factor in the pathogenesis of exogenous asthma and the cytokines played roles in the process of inflammatory reactions in the airway.

L12 ANSWER 12 OF 17 MEDLINE DUPLICATE 5
94009242 Document Number: 94009242. PubMed ID: 7691616. CD21 expressed on basophilic cells is involved in histamine release triggered by CD23 and anti-CD21 antibodies. Bacon K; Gauchat J F; Aubry J P; Pochon S; Graber P; Henchoz S; Bonnefoy J Y. (Glaxo Institute for Molecular Biology, Plan-Les-Ouates, Geneva, Switzerland.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1993 Oct) 23 (10) 2721-4. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Recombinant full-length **human CD23** incorporated into fluorescent liposomes was used to detect a ligand for CD23 on the basophilic leukemia cell line, KU 812. Based on our recent finding that CD23 interacts with CD21 on subsets of B and T cells, we investigated if the same ligand was involved on KU 812 cells. An anti-CD21 **monoclonal** antibody (mAb) BU-33, was able to totally block CD23-liposome binding to KU 812 cells. Moreover, KU 812 cells express CD21 mRNA and have a cell surface molecule that reacts with anti-CD21 mAb. The CD23/CD21 interaction was not merely physical but was also associated with an increase in histamine release by KU 812 cells. Both recombinant soluble CD23 and an anti-CD21 mAb-mediated effect on histamine release was not restricted to and anti-CD21 mAb-mediated effect on histamine release was not restricted to the leukemic cell line, but was also observed with normal human blood basophils. These data demonstrate that CD21 is expressed on basophilic cells and that CD21 controls histamine production upon ligand-induced stimulation (CD23 or anti-CD21 mAb).

L12 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
1993:470048 Document No. 119:70048 The mechanisms of **IgE** uptake by human alveolar macrophages and a human B-lymphoblastoid cell line (Wil-2wt). Richardson, D. R.; Cameron, K.; Robinson, B.; Turner, K. J. (Dep. Microbiol., Univ. West. Australia, Nedlands, Australia). Immunology, 79(2), 305-11 (English) 1993. CODEN: IMMUAM. ISSN: 0019-2805.

AB Human alveolar macrophages (HAM) internalized more **IgE** (81-) than human Wil-2wt B-lymphoblastoid cells (28-) suggesting a difference in the metabolic processing of the specific **IgE** receptor (CD23) or, alternatively, the presence of another functionally distinct receptor. The mannose receptor (MR), demonstrated to be present on the AM, may fulfill this role as **IgE** is heavily mannosylated and binds to a greater extent to Con A (which has specificity for oligomannose oligosaccharide chains) than other antibody isotypes. The hypothesis of a second **IgE** receptor was tested using mannan which is a competitive inhibitor of ligand binding to the MR and mannosylated bovine serum albumin (MBSA) which binds with avidity to the MR. Mannan (0.1 mg/mL) decreased internalized MBSA uptake in the HAM at 37.degree. suggesting the presence of the specific MR. In contrast, Wil-2wt cells did not bind MBSA. Mannan also reduced **IgE** uptake in the HAM at 37.degree. but had no effect on **IgE** uptake by Wil-2wt cells. Anti-CD23 **monoclonal** antibody (mAb) 135 also partially reduced membrane **IgE** uptake in HAM while completely inhibiting it by Wil-2wt cells. However, there did not appear to be competition for binding sites between **IgE** and MBSA in HAM. If only CD23 is involved in **IgE** uptake by HAM its function appears to be different to that in Wil-2wt cells. Definite involvement of the MR in **IgE** uptake will require further investigation as it may have an important role in allergic states.

L12 ANSWER 14 OF 17 MEDLINE DUPLICATE 6
93149192 Document Number: 93149192. PubMed ID: 1995115. Cytokine effects of CD23 are mediated by an epitope distinct from the **IgE** binding site. Mossalayi M D; Arock M; Delespesse G; Hofstetter H; Bettler B; Dalloul A H; Kilchherr E; Quaaz F; Debre P; Sarfati M. Groupe d'Immuno-Hematologie Moleculaire, CHU Pitie-Salpetriere, Paris, France. EMBO JOURNAL, (1992 Dec) 11 (12) 4823-8. Journal code: 8208664. ISSN:

0261-4189. Pub. country: ENGLAND: United Kingdom. Language: English.

AB **Human CD23** and its soluble forms (sCD23) display various biological activities, in addition to their **IgE** binding function (**IgE**/BF). The **IgE** binding domain was recently mapped to residues between Cys163 and Cys282 but its involvement in **IgE**-independent, CD23 functions remains unknown. In order to clarify this point, a series of N-terminal, C-terminal and internal deletion mutants of CD23 or sCD23 were expressed in CHO cells and tested for their ability (i) to bind to **IgE**, (ii) to induce colony formation by human myeloid precursor cells, (iii) to promote mature T cell marker expression by early prothymocytes, and (iv) to regulate **IgE** synthesis. The present study indicates that cytokine activities require the presence of Cys288, while this amino acid is not necessary for **IgE**/BF. Blocking experiments using various conformation-sensitive **monoclonal** antibodies further suggest that active epitope(s) of CD23 in cytokine assays is(are) distinct from those involved in **IgE**/BF.

L12 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS

1992:253891 Document No. 116:253891 Heterogeneity among Epstein-Barr virus-seropositive donors in the generation of immunoblastic B-cell lymphomas in SCID mice receiving human peripheral blood leukocyte grafts. Picchio, Gaston R.; Kobayashi, Ryo; Kirven, Marybeth; Baird, Stephen M.; Kipps, Thomas J.; Mosier, Donald E. (Div. Immunol., Med. Biol. Inst., La Jolla, CA, 92037, USA). Cancer Res., 52(9), 2468-77 (English) 1992. CODEN: CNREA8. ISSN: 0008-5472.

AB Epstein-Barr virus (EBV) is assocd. with B-cell malignancy in immunosuppressed humans and SCID mice receiving human peripheral blood leukocyte grafts (hu-PBL-SCID). Here, the process of lymphoma development was further characterized in hu-PBL-SCID mice. EBV-seropos. donors differ markedly in the capacity of their PBL to give rise to immunoblastic lymphomas in SCID mice; some donors (high incidence) generated tumors rapidly in all hu-PBL-SCID mice, other donors (intermediate-low incidence) gave rise to sporadic tumors after a longer latent period (>10 wk), and some donors failed to produce tumors. B-cell lymphomas arising from high incidence donors were multiclonal in origin, and EBV replication was detected in all tumors. Tumors derived from intermediate-low incidence donors were **monoclonal** or oligoclonal and often had no evidence of viral replication. All tumors, regardless of the donor, resembled EBV-transformed lymphoblastoid cell lines in surface phenotype but differed from lymphoblastoid cell lines by having less Epstein-Barr nuclear antigen 2 and CD23 expression. The variable patterns of lymphomagenesis seen among different EBV-seropos. donors may be explained by lower levels of specific immunity to EBV in high incidence donors, permitting activation of EBV replication and potential transformation of secondary B-cell targets. In addn. there may be differences in the transforming potential of EBV infecting different donors. The use of the hu-PBL-SCID model may help predict patients at high risk for posttransplant or AIDS-assocd. lymphomas.

L12 ANSWER 16 OF 17 MEDLINE DUPLICATE 7

92364541 Document Number: 92364541. PubMed ID: 1386872. Demonstration of a second ligand for the low affinity receptor for immunoglobulin E (CD23) using recombinant CD23 reconstituted into fluorescent liposomes. Pochon S; Graber P; Yeager M; Jansen K; Bernard A R; Aubry J P; Bonnefoy J Y. Glaxo Institute for Molecular Biology, Plan-Les-Ouates, Geneva, Switzerland. JOURNAL OF EXPERIMENTAL MEDICINE, 1992 Aug 1 176 2 399-97. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Recombinant full-length **human CD23** has been incorporated into fluorescent liposomes to demonstrate the existence of a ligand for CD23 that is different from the previously known ligand, immunoglobulin E (**IgE**). The novel ligand for CD23 is expressed

on subsets of normal T cells and B cells as well as on some myeloma cell lines. The interaction of full-length CD23 with its ligand is specifically inhibited by anti-CD23 **monoclonal** antibodies and by **IgE**, and it is Ca2+ dependent. Moreover, tunicamycin treatment of a CD23-binding cell line, RPMI 8226, significantly reduced the binding of CD23 incorporated into fluorescent liposomes, and a sugar, fucose-1-phosphate, was found to inhibit CD23-liposome binding to RPMI 8226 cells, suggesting the contribution of sugar structures on the CD23 ligand. In addition, CD23-transfected COS cells were shown to form specific conjugates with the cell line RPMI 8226. These data demonstrate that CD23 interacts with a ligand, which is different from **IgE**, and that CD23 can be considered as a new surface adhesion molecule involved in cell-cell interactions.

L12 ANSWER 17 OF 17 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 8
91341164 EMBASE Document No.: 1991341164. Expression of human recombinant CD23 in insect cells. Jansen K.U.; Shields J.; Gordon J.; Cairns J.; Graber P.; Bonnefoy J.-Y.. Glaxo Institute for Molecular Biology S.A. 46 route des Acacias, 1211 Geneva 24, Switzerland. Journal of Receptor Research 11/1-4 (507-520) 1991.
ISSN: 0197-5110. CODEN: JRERDM. Pub. Country: United States. Language: English. Summary Language: English.

AB **Human CD23** (low affinity receptor for **IgE**) has been expressed in insect cells (Sf9) using the baculovirus expression system and the baculovirus transfer vector pAc373. Insect cells infected with a recombinant baculovirus coding for CD23 synthesized a polypeptide not found in wild-type infected insect cells that had antigenic properties similar to natural CD23 produced in RPMI 8866 cells. Surface expression of recombinant CD23 was demonstrated by its ability to bind **IgE**. Recombinant CD23 expressed in insect cells had a slightly lower molecular weight (43 kDa) than that of natural CD23 (45 kDa) from RPMI 8866 cells as detected by SDS-PAGE followed by Western-blotting. Affinity-purified recombinant CD23 from infected insect cells showed B-cell growth promoting activity. These observations demonstrate for the first time that biologically active recombinant CD23 can be produced by the baculovirus expression system, thus providing a useful source of recombinant material to elucidate the biological functions of CD23.

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L1            15 S CHIMERIC CD23
L2             6 S L1 AND ANTIBOD?
L3             2 DUP REMOVE L2 (4 DUPLICATES REMOVED)
L4             1 S HUMANIZED ANTI CD23
L5        727044 S MONOCLONAL
L6            43 S L5 AND HUMAN CD23
L7             7 S L6 AND CHIMERIC
L8             3 DUP REMOVE L7 (4 DUPLICATES REMOVED)
L9             1 S L5 AND CHIMERIC CD23
L10            3 S L5 AND HUMANIZED CD23
L11           38 S L6 AND IGE
L12           17 DUP REMOVE L11 (21 DUPLICATES REMOVED)
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L14 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:320835 Document No.: PREV200000320935. Gamma-1 anti-**human** **CD23 monoclonal** antibodies. Reff, Mitchell E. (1); Kloetzer, William S.; Nakamura, Takehiko. (1) San Diego, CA USA. ASSIGNEE: IDEC Pharmaceuticals Corporation, San Diego, CA, USA; Seikagaku Corporation, Suita, Osaka, 565-0871, Japan. Patent Info.: US 6011138 January 04, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 4, 2000) Vol. 1230, No. 1, pp. No pagination. e-file. ISSN: 0098-1133. Language: English.

AB Anti-**human CD23 monoclonal** antibodies containing **human gamma 1** constant domains and therapeutic uses are provided. These antibodies inhibit IL-4 induced **IgE** production by B-cells significantly greater than antibodies containing other constant domains.

L14 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
2000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro **IgE** inhibition in B cells by anti-CD23 **monoclonal** antibodies is functionally dependent on the immunoglobulin Fc domain. Nakamura T; Kloetzer W S; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; Reff M E. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Feb) 22 (2) 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for **IgE** (FcvarepsilonRII), is involved in regulation of **IgE** synthesis by B-lymphocytes. Five **monoclonal** antibodies to **human CD23** were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of **IgE** complexes to CD23 positive cells and also inhibited the production of **IgE** in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) **monoclonal** antibodies. PRIMATIZED((R)) p5E8G1, containing **human gamma 1** constant region, inhibited **IgE** production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in **IgE** inhibition. An F(ab')(2) of p5E8G1 did not inhibit **IgE** production but did interfere with **IgE** inhibition by the intact anti-CD23 antibody in a dose dependent fashion. The murine **monoclonal** antibody MHM6 recognizes **human CD23** at a different epitope than primate antibody 5E8, and inhibits **IgE** production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit **IgE** production. These data imply that the mechanism by which anti-CD23 antibodies inhibit **IgE** production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit **IgE** production.

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
1999:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human** **CD23 monoclonal** antibodies and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO 9937199 A1 19990729, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,

BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.

AB **Monoclonal** antibodies which specifically bind **human CD23**, the low affinity receptor for **IgE** (FceRII/CD23), and contain either a **human gamma-1** or human gamma-3 const. domain, are disclosed. The antibodies are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the treatment or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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L15 9 IGE AND ALLERY

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L16 0 L15 AND ANTI HUMAN CD23

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L18 28761 L17 AND ALLERGY

=> s l18 and IgE
L19 4493 L18 AND IGE

=> s l19 and antibody
L20 2077 L19 AND ANTIBODY

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L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
2001:747174 Document No. 135:297587 Inhibitors for the formation of soluble **human CD23** and their use in **treatment** of diseases. Frey, Juergen (Germany). Eur. Pat. Appl. EP 1142910 A1 20011010, 29 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-107515 20000407.

AB A pharmaceutical compn. for the **treatment** or prophylaxis of disorders is described in which the overprodn. of sCD23 is implicated. This compn. comprises an inhibitor for the formation of human sol. CD23 which inhibitor decreases or blocks selectively the activity of the metalloprotease ADAM9 which otherwise mediates the shedding of sCD23 in human B-cell lines. Also described is a pharmaceutical compn. wherein the inhibitor for the formation of human sol. CD23 is a monoclonal or polyclonal **antibody** directed against the metalloprotease ADAM9 or wherein the inhibitor is an antisense oligonucleotide which is specific

for c-myc. Such a pharmaceutical compn. may be used in a method for selectively inhibiting the formation of ADAM9 as well as the formation of sCD23. It is a suitable medicament against inflammatory disorders, autoimmune diseases and **allergy**.

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
1998:604934 Document No. 129:215723 Gamma-1 and gamma-3 anti-**human** **CD23** monoclonal **antibodies** and use thereof as therapeutics. Reff, Mitchell E.; Kloetzer, William S.; Nakamura, Takehiko (Idec Pharmaceuticals Corp., USA; Seikagaku Corp. . PCT Int. Appl. WO 9837099 A1 19980827, 147 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US2253 19980217. PRIORITY: US 1997-803085 19970220.
AB Monoclonal **antibodies** which specifically bind **human** **CD23**, the low affinity receptor for **IgE** (FceRII/CD23), and contain either a human gamma-1 or human gamma-3 const. domain, are disclosed. The **antibodies** are useful for modulating or inhibiting induced **IgE** expression. Accordingly, they have practical utility in the **treatment** or prophylaxis of disease conditions wherein inhibition of induced **IgE** prodn. is therapeutically desirable, including allergic conditions, autoimmune diseases and inflammatory diseases.

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L24 11 L23 AND CD23 ANTIBODY

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L25 3 DUP REMOVE L24 (8 DUPLICATES REMOVED)

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L25 ANSWER 1 OF 3 MEDLINE DUPLICATE 1
2002224456 Document Number: 21957817. PubMed ID: 11962725. Anti-CD23 monoclonal antibody inhibits germline Cepsilon transcription in B cells.
Yabuuchi Shingo; **Nakamura Takehiko; Kloetzer William S** ; **Reff Mitchell E.** (Seikagaku Corporation, Central Research Laboratories, Higashiyamato, Tokyo, Japan.. yabuuchi@seikagaku.co.jp) . Int Immunopharmacol, (2002 Mar) 2 (4) 453-61. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.
AB A chimeric macaque/human (PRIMATIZED) anti-**CD23 antibody** , p6G5G1, demonstrated a strong inhibitory effect on IL-4 and anti-CD40 antibody-stimulated IgE production by human peripheral blood mononuclear cells (PBMCs) . RNA analysis by both reverse transcription-polymerase chain reaction (RT-PCR) and Northern blot showed that p6G5G1 inhibited germline Cepsilon RNA synthesis, but had no effect on CD23 mRNA levels. These data suggest that p6G5G1 may inhibit immunoglobulin class switching to IgE through the inhibition of germline Cepsilon RNA synthesis. Early addition of p6G5G1 after stimulation by IL-4 and anti-CD40 was critical for IgE inhibition. In contrast, later addition of p6G5G1 still showed inhibition of increased levels of surface CD23, which is normally upregulated by stimulation with IL-4 and anti-CD40.

L25 ANSWER 2 OF 3 MEDLINE DUPLICATE 2
20000150073 Document Number: 20150073. PubMed ID: 10684997. In vitro IgE inhibition in B cells by anti-CD23 monoclonal antibodies is functionally dependent on the immunoglobulin Fc domain. **Nakamura T**; **Kloetzer W S**; Brams P; Hariharan K; Chamat S; Cao X; LaBarre M J; Chinn P C; Morena R A; Shestowsky W S; Li Y P; Chen A; **Reff M E**. (Seikagaku Corporation, Tokyo Research Institute, Tokyo, Japan.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000 Feb, 22 (2): 131-41. Journal code: 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD23, the low affinity receptor for IgE (FcvarepsilonRII,), is involved in regulation of IgE synthesis by B-lymphocytes. Five monoclonal antibodies to human CD23 were generated from cynomolgus macaques immunized with purified soluble CD23 (sCD23). Four of the five primate antibodies blocked the binding of IgE complexes to CD23 positive cells and also inhibited the production of IgE in vitro by IL-4 induced human peripheral blood mononuclear cells (PBMC). The variable domains of several primate antibodies were utilized to construct chimeric macaque/human (PRIMATIZED((R))) monoclonal antibodies. PRIMATIZED((R)) p5E8G1, containing human gamma 1 constant region, inhibited IgE production in vitro as efficiently as the parent primate antibody, but the human gamma 4 constant version, PRIMATIZED((R)) p5E8G4, was not as effective in IgE inhibition. An F(ab')(2) of p5E8G1 did not inhibit IgE production but did interfere with IgE inhibition by the intact anti-**CD23** **antibody** in a dose dependent fashion. The murine monoclonal antibody MHM6 recognizes human CD23 at a different epitope than primate antibody 5E8, and inhibits IgE production by IL-4 induced PBMC. As with the F(ab')(2) of p5E8G1, the F(ab')(2) of MHM6 also failed to inhibit IgE production. These data imply that the mechanism by which anti-**CD23** **antibodies** inhibit IgE production requires cross-linking of CD23 to an IgG receptor. These data also imply that neither bivalent cross-linking of CD23 alone or inhibition of CD23 binding to its natural ligands is sufficient to inhibit IgE production.

L25 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
1999:779157 Document No. 132:19632 Method for integrating genes at specific sites in mammalian cells via homologous recombination and vectors for accomplishing the same. **Reff, Mitchell R.**; Barnett, Richard Spence; McLachlan, Karen Retta (Idec Pharmaceuticals Corporation, USA). U.S. US 5998144 A 19991207, 43 pp., Cont.-in-part of U.S. 5,830,698. (English). CODEN: USXXAM. APPLICATION: US 1998-23715 19980213. PRIORITY: US 1997-819866 19970314.

AB A method for achieving site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. This method provides for the reproducible selection of cell lines wherein a desired DNA is integrated at a predetd. transcriptionally active site previously marked with a marker plasmid (Desmond). This unique site may be bacterial DNA, a viral DNA or synthetic DNA. This Desmond marker plasmid contains the Salmonella HisD gene, the Neomycin phosphotransferase exon 3, the murine dihydrofolate reductase, cytomegalovirus and SV40 enhancers, splice acceptor site, mouse beta globin major promoter, bovine growth hormone polyadenylation site, SV40 early and late polyadenylation sites. The selectable marker proteins may include neomycin phosphotransferase, histidinol dehydrogenase, dihydrofolate reductase, hygromycin phosphotransferase, HSV thymidine kinase, adenosine deaminase, glutamine synthetase, and hypoxanthine-guanine phosphoribosyl transferase. Marked CHO cells were produced and characterized. Other cells that may be marked include myeloma cells, baby hamster kidney cells, COS cells, NSO cells, HeLa cells and NIH 3T3 cells. The method is particularly suitable for the prodn. of mammalian cell lines which secrete mammalian proteins at high levels, in particular Igs. Novel targeting vectors "Molly" and vector combinations for use in the subject cloning method are also provided. This Molly vector contains dihydrofolatereductase, Ml-Neomycin

phosphotransferase exon1, N2+Neomycin phosphotransferase exon 2, anti-CD20 light chain leader+variable, human kappa const., anti-CD20 heavy chain leader+variable, human gamma 1 const., Salmonella histidinol dehydrogenase, CMV and SV40 enhancers, SV40 origin, splice donor/acceptor, CMV promoter/enhancer, HSV TK promoter and poloma enhancer, mouse beta globin major promoter, SV40 late polyadenylation, bovine growth hormone polyadenylation. Expression of an Anti-CD20 and Anti-human **CD23 antibody** and immunoadhesin in Desmond marked CHO cells was achieved.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	113.11	113.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58

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